AIR POLLUTANTS AFFECTING THE PERFORMANCE OF DOMESTIC ANIMALS

A Literature Review

Agriculture Handbook No. 380

Agricultural Research Service
UNITED STATES DEPARTMENT OF AGRICULTURE

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By ROBERT J. LILLIE,
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Animal Science Research Division

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AIR POLLUTANTS AFFECTING THE PERFORMANCE OF DOMESTIC ANIMALS—

A Literature Review

Chapter 1.—Introduction

By ROBERT J. LILLIE, *research poultry husbandman,*
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Expansion of industrialization and urbanization has contributed greatly to the rise in the incidence of pollution in the environment, which prompted an investigation on the overall picture of environmental pollution. The results were summarized and submitted to the President of the United States.[1] That report was primarily on human beings, with some discussion on marine life and zoo animals. Since that report contained very little information on farm animals, a literature survey was conducted to determine the effects of air pollution on domestic animals. The results are presented herein.

The term "domestic animals" as used in this report includes cattle, sheep, goats, swine, horses, chickens, turkeys, ducks, geese, pigeons, Japanese quail, dogs, cats, rabbits, and honey bees. Whenever the literature survey indicated a paucity of information on the effects of certain air pollutants on domestic animals, data obtained with laboratory animals, wildlife, and humans exposed to the said pollutants are included in the report because of the possible applicability to domestic animals.

Several difficulties have been encountered in the literature survey, such as the screening of thousands of publication titles relevant to air pollution and domestic animals, the location of certain references, the differentiation between sources of poisoning in the domestic animal, and the interpretation of the published results. Many references were not included in the literature survey because of insufficient information on the concentration of pollutant, type of exposure, and length of exposure.

Chapters 2, 3, and 4 on air pollution, smoke, and automobile exhausts provide a brief background on the generalities of these pollutants and their effects on domestic animals. Many of the specific air pollutants found in the air, smoke, and automobile exhausts are described in subsequent chapters, which contain a brief introduction of the air pollutant, the published results, a summary, and a bibliography. For the sake of simplicity and clarity, the published results were subdivided on the basis of exposure type (inhalation, ingestion, injection), observation (field, laboratory), and species of animal. No attempt was made to evaluate the reliability of data in the literature survey. However, in several cases, the writer made notations in parentheses about some of the published data.

Literature references are placed at the end of each chapter. Italic numbers in parentheses refer to the literature cited for the chapter.

The literature survey is not complete. The survey was discontinued October 1, 1968, with many references not yet available from the libraries. Other references may have been inadvertently overlooked.

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[1] HORNIG, D. F., AND OTHER MEMBERS OF THE PRESIDENT'S SCIENCE ADVISORY COMMITTEE. RESTORING THE QUALITY OF OUR ENVIRONMENT, Environmental Pollution Panel Rpt., the White House, November 1965.

Chapter 2.—Air Pollution

Urbanization and industrialization have expanded tremendously and consequently have increased the flow of pollutants into the atmosphere, soil, and water. The management practices adopted in urban and industrial areas, in the meantime, have not kept up with the ever-increasing quantities of pollutants. The result was an excess of pollutants that began to exert detrimental effects on man, animals, and plants. Some of the effects of air pollution on man, plants, and animals have been comprehensively reviewed (*2, 5, 13, 23, 30, 34, 41, 48, 49, 50, 52*). In these reviews, a majority of the animals represented laboratory animals; however, some reviews discussed effects of arsenic, fluoride, lead, molybdenum, and sulfur dioxide on livestock (*2, 13, 50*). Of all the pollutants studied, the fluorides were the only pollutants that were well defined in the literature with respect to livestock (*13*). One reviewer (*49*) reported that of all known air pollutants, economic poisons, chiefly from ingestion of contaminated vegetation, posed the greatest current threat to the health of wildlife. Another reviewer in 1967 (*34*) said:

> In my travels and reading, I sought information on how air pollution affects animals. I found very little, except in studies on laboratory animals. Reports of animal deaths during the major air pollution episodes are fragmentary and inconclusive. Some post-mortem studies are being made on deceased pets in cities with chronic pollution problems. A Japanese zoo reports that air pollution is a factor in more than one-third of their animal deaths, but this statement is too general to command confidence.

MAJOR AIR POLLUTION EPISODES

The major air pollution episodes that affected man and animals including domestic animals in Donora, Pa., London, Poza Rica, Meuse Valley, and New York City have been reviewed (*13, 22, 23, 28, 38, 44, 48*). During the London fog of 1952 prized fat cattle succumbed to the effects of the fog at the Smithfield Club's show; the clinical symptoms were increased respiration, dyspnea, raised body temperature, refusal to eat, death; the pathological examination revealed acute bronchiolitis, emphysema, and right heart failure (*22, 23*). Sheep and swine were not affected; some of the slaughtered cattle were passed as fit for food (*22*). A similar episode had occurred at the same club in 1873 in which cattle, but not sheep nor swine, were affected (*1*). Hence, an anatomical or physiological peculiarity might account for a species difference (*22*).

Analysis of data obtained with domestic animals exposed to the Donora, Pa., smog suggested a positive correlation between the smog and health of small domestic animals (dog, cat, poultry, rabbit) (*44*). Four retail milk plants in the Donora area reported no significant drop in milk production during or after the smog period; no unusual illness was observed by local veterinarians, poultry dealers, slaughterhouse officials, and local dairy cattle breeding associations with the animals under their charge.

Particulars on some major air pollution episodes are further discussed in chapters on hydrogen sulfide and sulfur dioxide.

SOURCES

Sources of air pollution, although varied, can be narrowed to three general categories: nature-made, man-made, and animal-made. In the nature-made category are volcanic gases (*16*) and dusts, pollen, viruses, fungi, and bacteria (*29*); the man-made category includes smoking, home fires (*4*), industrial plants (*9, 15, 20, 24, 43, 45*), motorized traffic (see chapter 4), and pesticides and radioactive contaminants, both of which were excluded in the literature survey; the animal-made category represents farms and other areas where animals create a source of regional atmospheric air and soil pollution (ammonia, nitrites, nitrates, hydrogen sulfide, chlorides, flies, micro-organisms, odors, fecal matter) (*10, 11, 25*).

TOXICOLOGY OF AIR POLLUTANTS

The toxicity of air pollutants is largely influenced by many variables: type and concentration of pollutant, prevailing winds, temperature, humidity, rainfall, topography, season, species, age, management and activity of animals, length of exposure, nutrition, genetics, physiology, and others. Many of these variables are discussed elsewhere in the report. Toxicity in animals may be of the acute or chronic form. The acute form usually refers to inhalation of large quantities of an air pollutant or ingestion of heavily contaminated vegetation, resulting in death; the chronic form refers to the inhalation of sublethal levels of an air pollutant or to ingestion of low levels of contaminated vegetation for long periods.

A strong relation between local air pollution and incidence of diseases (primarily carcinogenic lesions) has been reported in humans (*17*), in zoo animals (*27*, *47*), and in dogs (*32*). Since the data with humans revealed that mouth breathers were more prone to dental and lip lesions than nose breathers it would be interesting to observe what the effects would be on dogs that pant in hot weather. The immunobiological response of animals exposed to various diseases (typhoid, anthrax, tuberculosis, *Staphylococcus aureus*, and others) has been lowered in the presence of industrial air toxicants (*18*). More information is needed on the role of air (clean vs. polluted) in the transmission of disease (*21*).

CLEAN VERSUS POLLUTED ATMOSPHERES

Different species of animals were exposed to ambient Los Angeles air with contrasting patterns of atmospheric pollution (densely vs. lightly polluted areas) (*12*, *14*). In some cases, the ambient air was filtered through activated charcoal. Dogs and chickens exposed to the densely and lightly polluted areas showed no significant changes in their health status, behavior, and growth.

Exposure to a man-created photochemical smog in inhalation chambers produced more deleterious effects on the respiratory system than a photochemical smog occurring in the field (*14*). Differences in data obtained in field and laboratory environments may be attributed to interactions of many factors necessary to produce critical physiological and pathological situations (*13*).

Despite the public concern for the polluted atmosphere and its effects on life, unfiltered ambient air does have some merit, at least in one study with rats (*46*). The study involved two environments: ambient (normal) and controlled (in which the ambient air was filtered before entry). One group of rats was fed a laboratory chow ration and another group an amino acid basal purified diet in both environments. The data showed that the amino acid basal diet induced a trace-element deficiency in the controlled environment only. The symptoms were alopecia, seborrhea, and growth retardation within 1 to 3 weeks; and death occurred within 2 to 6 weeks. The active element(s) missing in the amino acid basal diet were found to be supplied by impurities in the unfiltered ambient air. This report should open up an entirely new field in the area of environmental-nutritional research. For instance, would the nutritional requirements established under ambient conditions for domestic animals be altered by polluted air?

INHALATION VERSUS INGESTION

Air pollutants enter the body of the domestic animal via inhalation or ingestion of contaminated vegetation. For herbivorous animals, the ingestion of contaminated vegetation within a grazing zone of pollution is probably more important than inhalation because greater quantities of an air pollutant per unit body weight enter the body via ingestion than inhalation (*13*, *36*, *40*). Some pollutants may be absorbed through the integument or ingested by licking or grooming of hair or feathers. Prolonged exposure of vegetation before ingestion might result in an accumulation of toxic amounts of the contaminant from the atmosphere that itself is not particularly harmful by inhalation (*6*, *26*, *51*).

Nevertheless, practically no information was available in the literature to determine the degree of intoxication resulting from the inhalation of the pollutant and from the ingestion of vegetation contaminated by the same pollutant in the same domestic animal at the same time.

PHYSIOLOGICAL EFFECTS OF AIR POLLUTION

As contrasted with humans, there has been no occasion to distinguish between toxic and sensory effects in farm animals. Overt behavior as well as objective signs (tear section, inflammation of eyes and mucous membranes) might indicate a sensory response to painful substances, whereas, the systemic toxic effects would consist of chemical and morphological changes of tissues indistinguishable in general from those observed in humans (*6*).

The interaction of a foreign compound (air pollutant) and the animal body's enzymes represents any one of the five biochemical consequences: oxidation, reduction, hydrolysis, synthesis, and no change (*54*). The first four biochemical consequences could represent any one of the three metabolic transformations: A nontoxic compound may become toxic, a toxic compound may be detoxicated, or a toxic compound may be changed into another toxic compound with the same or different toxic action. The enzymatic activity varies with species, sex, strain, and age of animals.

The inhalation of chemicals initiates responses that can be grouped into four areas: (a) airways that respond by bronchoconstriction to initiate the cough reflex, (b) bronchial blood vessels that undergo changes to reduce absorption of the chemicals via the bronchial mucosa, (c) pulmonary blood vessels that respond to reduce absorption of the toxic irritants via the alveolar capillaries, and (d) heart and systemic vessels that retard the distribution of the chemical substance to the vital organs. Pollutants behave differently in the four areas: SO_2 exerts its primary effects on the airways; NO_2 and O_3, on pulmonary capillaries; CO, on circulation; and HC, on blood vessels (*8*). Another area that should not be overlooked is the pollutant interference with the clearance mechanisms of the pulmonary system, such as the ciliary and alveolar macrophage. Alterations of the clearance mechanisms in most instances are more important factors in the toxicological and physiological effects of air pollutant than airway or vascular changes.[1]

Laboratory studies (*49*) have revealed three rather general phenomena associated with exposure to air pollutants: (a) synergism—the potentiated toxic effect of combination of certain compounds—and its converse, antagonism—in which the summated toxicity is either far less than predicted or nonexistent; (b) tolerance and cross tolerance to pulmonary edema-producing agents; and (c) the immunochemical response.

PROBLEMS INVOLVED IN VETERINARY DIAGNOSIS

The differentiation of diseases created by air pollutants from diseases caused by environmental stresses (nutritional disorders, poor husbandry practices, parasitism, airborne pathogens, and others) can be rather difficult for the veterinarian. Diagnosis of air pollution diseases in farm animals should include the identity and concentration of pollutant(s) in the affected area, a comparison of the clinical and pathological symptoms of affected animals with those of the same species given a similar dosage level in the laboratory, a comparison of the overall performance of the animals in affected and unaffected areas, a thorough investigation of the structural changes within the animal body, and the degree of toxicity (acute vs. chronic).

The methods of using atmospheric analysis data to predict effects of air contaminants on farm animals should be used with caution by the veterinarian until the deficiencies in the analytical methods and understanding of the problems are overcome (*33*). However, standardization of methods for measurement of air pollutants to reconcile differences and to demonstrate the accuracy of currently available methods of air analysis is becoming a reality (*42*).

Veterinary diagnosis is a highly interdisciplinary

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[1] Personal communication from T. R. Lewis, National Air Pollution Control Administration, Consumer Protection and Environmental Health Service, Public Health Service, U.S. Department of Health, Education, and Welfare. 1969.

subject with a strong dependence on pharmacology, physiology, pathology, biochemistry, and anatomy. Only a few substances have been studied in great detail in such a way that cellular and subcellular effects are known as well as their interplay in the whole organism (*31*). The structural and cellular changes in emphysematous horse lungs have been thoroughly described (*19*). Little information is available on the question of adaptation, because the procedures of studying the effects for long periods and at various levels of exposure are expensive and tedious (*31*). Such effects may become immeasurable, especially with low concentrations of air pollutants. For instance, pathological changes may not be apparent at low concentrations but might become apparent if the subject is exposed to a challenge with an airborne infectious micro-organism (*7*).

Differentiation between atmospheric and nonatmospheric poisons is important, because certain poisons, such as arsenic, fluoride, and lead, can be either atmospheric or nonatmospheric in origin. Treatment of animals poisoned from nonatmospheric sources is much easier than from atmospheric sources. Examples of some nonatmospheric poisons have been described (*55*). Since a veterinarian may not be cognizant of all the disciplines involved in air pollution and in treating its effects upon farm animals, he should specialize in air hygiene along with veterinary medicine (*5*). The complete validity of this statement remains to be challenged.

LEGISLATION

Legislation against air pollution took place as early as 1306 in England (*37*) and early in old Russia, where a number of litigations developed between the owners of industrial plants and "pomeshchiks" (rich landlords) because of the damage inflicted on the surrounding agricultural husbandry (*41*). Even though the air pollution concentration was lower in Sweden than in England, the Swedish became interested in air pollution control measures because the advancing urbanization and industry had some deleterious effect on plant and animal life (*35*). As of 1965, 30 of the 50 States in the United States had air pollution laws pending, with another 7 States having either water or general pollution laws pending (*3*). The suggestion that analyses of air, plant, and soil samples be made before a new factory goes into operation to provide a measure of determining the degree of damage later on as a result of atmospheric pollution was recommended in Holland (*53*).

EFFECTS OF CLEANED AIR

According to the Committee on bird sanctuaries in the Royal Parks, house martins that had not nested for 80 years in London, once the most polluted major city in the world, returned after the revival of the insect populations. It was undoubtedly The Clean Air Act of 1956, which restricted the free burning of coal in hearths and fireplaces, that permitted the revival of the insect population (*4*).

RESEARCH PROJECTS AND IDEAS ON AIR POLLUTION

A list[2] of State experiment stations actively or inactively engaged in research projects on effects of air pollution on domestic animals showed the following areas of work: Alabama, Maine, and Maryland on environmental requirements for poultry; Illinois on volatile pollutants with swine; Tennessee on atmospheric effluents affecting cattle; Utah on fluoride-enzyme interactions in animal tissues; and Wisconsin on fluoride toxicity with cattle.

Research ideas and speculations on the effects of air contaminants on the performance of poultry and swine were submitted by an investigator who was interested in the overall picture of air pollution in animal husbandry (*39*). (Note: Some of his questions have already been answered; others should be, especially those questions regarding the effect of continuous presence of air contaminants on the flavor of meat of broilers and pigs.) Research investigators should not rely too much on some of the published results relevant to air pollution, because many of these results may not be true or may be misleading. In fact, one investigator termed some of the results facts and fables (*37*).

[2] Personal communication from A. J. Loustalot, principle plant physiologist, Cooperative State Research Service, U.S. Department of Agriculture. Washington, D.C. 1968.

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Chapter 3.—Smoke

Smoke is defined as gaseous products of burning organic materials, such as wood, coal, peat, tobacco, oil, and gas. The smoke emissions that contaminate the atmosphere may or may not be visible and may or may not contain many constituents that are detrimental to domestic animals as well as wildlife (*4, 5, 6, 10, 12, 17, 18*).

To be able to prove damage incurred from industrial smoke, one must have chemical proof of the presence of an active poison in the smoke and the same in the organs of the stricken animal. However, this proof is insufficient for any evaluation of damage to the health and economic value of the animal. Other factors needed for such evaluation are: clinical and pathological observations of the animals, comparison of exposed animals with those in nonexposed areas, and observation of the actual smoke distribution. The only real safety measure against the dangers of smoke lies in the complete removal of toxic constituents in the smoke being emitted into the atmosphere (*13*). Despite control measures adopted by industry, poisons are still being emitted by industry. In many cases, the poisoning is very difficult to attribute to a specific factory; and, therefore, a suit cannot be brought to court (*17*).

BIOLOGICAL EFFECTS OF SMOKE FROM DIFFERENT SOURCES

Smoky Atmosphere

Livestock

Because of the poor quality of vegetation and also because of the smoky atmosphere, sheep raising was almost an impossibility in the Yorkshire, England, area; the wool was of very poor quality and full of impurities of various kinds. Growth of other farm animals was affected; they appeared to require more attention and food than those in a clean area (*1*). Ewes in the Yorkshire area exhibited a greater incidence of abortion than normally expected (*11, p. 91*). In the Lancashire, England, area 1 acre of ground supported two cows before the age of smoky atmosphere, as contrasted with 3 acres per cow since the increase in smoky atmosphere. The milk of affected cows was deficient in calcium (*2*).

Wild animals

Wild animals including birds living in the London Zoo for many years developed carbon deposits (necrotic foci) in the lungs that culminated in death as a result of breathing the smoky atmospheres (*3; 11, p. 70*). Hares living in the smoky areas frequently died of dysentery (*11, p. 91*).

The presence of tarry deposits in the smoky atmosphere inhibited growth of many plants with a consequent decrease in the population of insects that fed on the plants and a corresponding decrease in the population of birds that fed on the insects (*11, pp. 85–86*).

Certain moths have a tendency to produce black or blackish variants (melanism) in a normal atmosphere. The conspicuous color makes the moths more easily destroyed by predators. However, in smoky areas, these moths produce sooty colors instead of black, which is less conspicuous; thereby, these moths increase at the expense of normal-colored moths (*11, pp. 91–92*).

Smoke From Asphalt Plants

Cattle and sheep

In three adjoining farms near an asphalt boiling plant, illness and death occurred in cattle and sheep (*8*). The clinical symptoms were: slight rise in temperature, rapid pulse, loss of appetite, vomiting, tympanites, and dark viscous feces with a pungent smell. The pathological picture showed a heavy accumulation of blood in the omentum, edematous wall of the proventriculus, hyperemic mucous membranes of the intestine, and enlarged liver with a lighter color and with dark delineations. The histological examinations showed heavy necrotic changes of the liver and hemorrhage in the kidneys. Chemical analysis of the organs, urine, stomach contents, and stomach wall revealed comparatively large amounts of phenol.

Poultry

Egg production had dropped 50 percent and death or disease had struck 59 percent of the hens kept in several henneries containing over a thousand Leghorn layers near an asphalt factory in Japan (*9*). Pathological findings showed congestion; hemorrhage or catarrh in ovaries, gullet, trachea, lungs, and intestine; and kidneys enlarged by $1\frac{1}{2}$ to $2\frac{1}{2}$ times the normal size. Laboratory tests ruled out bacterial and viral infections. The asphalt soot exposure test produced similar results; thereby, the blame was put on the soot from the asphalt factory. The poisonous constituent in the soot was not identified.

Smoke From Coal

Rabbits and rats were exposed for 80 days in closed chambers to bituminous coal smoke containing an average of 125 million particules per cubic foot, of which only 0.4 million particles were free silica dioxide (*15*). Some animals were sacrificed after 80 days of exposure; and others retained in a normal atmosphere, for another year. The pathological symptoms of animals sacrificed at the termination of the 80-day exposure included deeply pigmented lungs, presence of black pigment distributed throughout the lungs, bronchitis and bronchopneumonia in some cases, and enlarged, blackened peribronchial lymph nodes. The other animals retained for over a year developed fibrous reactions around the carbon deposits with formation of collagen strands, typical of bituminosis seen in soft coal miners.

Smoke Containing Soot and Fly Ash

Inhalation of soot leads to anthracosis, whereas, ingestion of soot with food has no effect; inhalation of fly ash (soot) could lead to pneumoconiosis, not commonly observed in animals; the effect of ingestion of fly ash on bones is complex and influenced by mechanical, chemical, and physical effects (*6*).

Up to 2 kg. of raw ash could be ingested with 10 kg. of meadowgrass daily without adverse effects on domestic animals (*14*).

ESTHETIC EFFECTS OF SMOKE

The esthetic effect of smoke was most pronounced with light-colored or white animals, in which the normal color became "tattle-tale gray" or dusky gray like a mouse. Exhibitors of prized animals were deeply concerned because frequent soapy water baths did not entirely remove the smoky film from the coat hair or feathers (*3; 7; 16, p. 75*).

SUMMARY

Smoky areas become undesirable for grazing because of the poor quality of vegetation and inhalation of smoke. Cases of abortion in sheep, poor-quality wool, increased acreage required per cow, extra feed and attention needed for adult livestock, stunted growth of young livestock, calcium deficiency in bovine milk, decreased egg production, and high mortality in layers, illness and death in sheep and cattle exposed to phenol from asphalt smoke, and soiled coat hair or feathers of prized exhibition farm animals have been reported in smoky areas.

Carbon deposits from coal smoke have been responsible for deaths among zoo wildlife. Survivors develop fibrosis around the carbon deposits, typical of bituminosis in soft coal miners. Inhalation of fly ash (soot) leads to anthracosis or pneumoconiosis or both in humans, which is uncommonly observed in animals. Ingestion of fly ash may be influenced by mechanical, chemical, and physical effects, although small quantities of fly ash could be eaten without apparent harm.

A reduction in the insect population with a corresponding decrease in the population of birds that fed on the insects and a change from black spots to sooty-colored spots in certain moths have been observed in smoky areas.

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Chapter 4.—Automobile Exhausts

Automobile exhaust fumes containing carbon monoxide, hydrocarbons, nitrogen dioxide, sulfur dioxide, lead, aldehydes, and other compounds are recognized as a major air pollutant, especially in metropolitan areas. In spite of the tremendous mileage of highways being constructed to accommodate the ever-increasing volume of vehicular traffic, no information could be found in the literature on the effect of inhaled automobile exhaust gases on domestic animals except dogs (ch. 15). The biological effects of engine exhausts on laboratory animals were briefly reviewed (*12*). Some of these effects will be described to give an indication of what might happen to exposed domestic animals.

FACTS ABOUT AUTOMOBILE EXHAUSTS IN THE NATURAL ENVIRONMENT

In a study (*3*) it was found that for an automobile traversing Los Angeles county through residential, industrial, downtown, and high speed semirural areas during periods of both peak and nonpeak traffic, 18 percent of the time the engine was idling, 18 percent decelerating, 18 percent accelerating, and 46 percent cruising. The quantity of polycyclic HC and soot emitted was maximal on acceleration; the amount of uncombusted gasoline liberated through the exhaust was maximal during deceleration, followed by idling. Pyrene was present in largest quantities in all hydrocarbon samples obtained from the automobile exhausts, followed by benzene derivative.

Although the diesel-engine exhaust did not differ markedly from gasoline-engine exhaust, the diesel-engine exhaust was a greater source of hydrocarbon pollution in the atmosphere than the gasoline exhaust engine; furthermore, the diesel-engine exhaust contained more carcinogenic hydrocarbons than the gasoline-engine exhaust (*4*). As the load and engine speed of the diesel engine were increased, the emissions of aromatic polycyclic hydrocarbon were increased; the reverse was true for gasoline engines.

Analysis (*10*) of the air of 14 American cities revealed the presence of pyrene and benzene and their derivatives as well as several other hydrocarbons; the concentration usually was greater in the winter than in the summer. Engine exhausts were believed (*1*) to be one of the contributing factors in the development of pulmonary diseases and subsequent death in zoo animals.

EXPOSURE TO AUTOMOBILE EXHAUST INHALATION IN THE LABORATORY

Dogs

Four mongrel dogs fed a standard meal were exposed to diesel-engine fumes in a closed chamber every day for 15 minutes for a 5- to 8-week period (*11*). The clinical symptoms included anorexia, dermatitis, conjunctivitis, scleritis, ulceration of legs, emaciation, dullness, tonic and clonic convulsions, emphysema and pulmonary edema; the pathological examinations after death revealed lung and liver congestion. The data prompted the authors to suggest that apartment developments not be constructed in the vicinity of heavy motor traffic because of vehicular pollution of the atmosphere.

Laboratory Animals

Automobile exhaust gases

The chief toxic constituents of automobile exhaust gases obtained from a single-cylinder diesel engine running under four different conditions were (*8*): acrolein and to a lesser extent NO_2 under light running load; NO_2 under moderate load; a lower NO_2 content under moderate load with a worn injector; and CO and to a lesser extent irritants under light load with the air intake restricted. Very little black smoke occurred in the exhaust under the four running conditions. Death occurred among mice, guinea pigs, and rabbits, in most, if not all, cases between 5 and 7 hours of exposure. The pathological symptoms represented gross damage to the entire respiratory tract such as edema, emphysema, and congestion.

When the automobile exhaust fumes were blended with air and irradiated to simulate the effects of sunlight in the natural environment, the resulting irradiated automobile exhaust gases became more potent than nonirradiated gases, as measured by pulmonary function and spontaneous activity (*2*, *6*, *7*), by mortality (*7*), by increased CO hemoglobin (*6*), and by decreased fertility and survival rate of progeny of mice (*2*). The approximate concentration needed to produce 50 percent depression of activity in mice was 2,700, 7,100, 250, 0.3, 16, and 0.4 p.p.m. for irradiated, nonirradiated exhaust, CO, O_3, NO_2 and acrolein, respectively (*6*). Most of the effects rapidly returned to preexposure normal when the rodents were provided with fresh air (*7*).

The use of automobile exhaust gases as a fumigant in grain storage bins was highly effective in killing rodents (*9*).

Automobile exhaust oil particles

Mice, rats, rabbits, and monkeys were exposed for intervals ranging between 100 and 365 consecutive days to fogs composed of ordinary automobile oil particles (*5*). Lipid pneumonia was not a hazard for rabbits, mice, and rats in atmospheres containing 63 to 132 mcg. oil/l. of air because the low pulmonary retention enabled the phagocytes of the lung to engulf and remove the oil mist adequately. Monkeys exposed to oil fog, however, were more susceptible to infectious pneumonia than control monkeys.

EXPOSURE TO AUTOMOBILE EXHAUST GAS INGESTION

Barley and oats obtained from grain storage bins fumigated with automobile exhaust gases to kill rodents used as a feed supplement did not affect swine and asses (*9*). A cereal made from such grain was palatable.

SUMMARY

Although several domestic animals (dogs, rabbits) were tested in a laboratory, no information could be found in the field about the effect of inhaled automobile exhaust gases from ever-encreasing numbers of vehicles on domestic animals living near heavily traveled highways. The construction of apartment developments near the vicinity of heavy motor traffic was not recommended because of the presence of carcinogenic hydrocarbons in automobile exhausts.

The ingestion of barley and oats fumigated with automobile exhaust gas did not affect swine and asses. Such fumigation was highly effective in destroying rodents inhabiting the grain storage bins.

Experimental research data revealed lung and liver congestion, dermatitis, conjunctivitis, scleritis, anorexia, convulsions, reduced fertility and progeny survival rate, and death in laboratory animals.

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Chapter 5.—Ammonia

Ammonia (NH_3) is formed when nitrogenous organic matter is heated in the absence of air. Hence, NH_3 has been liberated from coal and oil-bearing shale, both of which are rich in nitrogenous matter. No information was found in the literature survey about the effect of industrial NH_3 on domestic animals with one exception (*14*): NH_3 was found to lower the immunobiological activity of rabbits, pigeons, man, and rodents against typhoid fever, anthrax, and other diseases.

However, a preponderance of literature referred to atmospheric NH_3 produced by the animals themselves, particularly, poultry. Other references pertained to exposure of animals to various levels of NH_3 in an environmental chamber.

EXPOSURE TO NH_3 IN THE FIELD

Poultry

Content in the atmosphere

Air samples from broiler houses were analyzed for NH_3 and contained a range of 0.060 to 0.009 mg./l. (60 to 9 mg./m.^{3}) of air with an average of 0.033 mg./l. (33 mg./m.^{3}). No disorders clearly attributable to NH_3 could be observed (*25*). NH_3 production depends on the amount of fecal matter in the litter, litter moisture, temperature, humidity, ventilation, floor space per bird, and season (*5, 17, 18, 21, 23, 26, 27, 28*). An increase in NH_3 concentration is associated with high temperature, high humidity, poor ventilation, overcrowding, and cold weather.

Symptoms

With day-old chickens the symptoms usually became apparent by the fifth week of age. The symptoms included watery eyes, closed eyelids, rubbing of eyes on the wing, decreased growth rate, poor feed conversion, huddling together of affected birds (*17, 23, 26, 28*). Levels up to 75 p.p.m. (52 mg./m.^{3}) did not retard growth but induced an unhealthy appearance (*18*).

The pathological symptoms involved the erosion of the cornea of the eye, more commonly known as keratoconjunctivitis (*2, 5, 23, 26, 28*). In two cases 60 p.p.m. NH_3 (42 mg./m.^{3}) was needed to produce keratoconjunctivitis (*18, 27*). Whenever the concentration fell below 60 p.p.m. the rate of recovery from the eye disorder depended on the severity of the ulcers (*26*). Attempts to reproduce keratoconjunctivitis in healthy chicks with material from affected birds in the field were unsuccessful (*28*).

Resistance to disease

Excessive quantities of NH_3 (50 p.p.m. (35 mg./m.^{3}) and above) for prolonged periods predispose chickens to respiratory diseases with the added risk of secondary infections (*17, 26, 27*). Lower levels (8 p.p.m.) (6 mg./m.^{3}) or 20 to 30 p.p.m. NH_3 (14 to 21 mg./m.^{3}) for 10 weeks did not significantly increase the incidence of air sacculitis in turkey poults (*12*).

In another case (*2*) exposure of chickens from 0 to 16 weeks of age to a very highly concentrated NH_3 atmosphere, as a result of active decomposition of accumulated droppings, did not significantly increase the incidence of leucosis up to 1 year of age. Keratoconjunctivitis developed in 25 percent of the birds by the 16th week of age; the removal of affected chickens to clean, well-ventilated rooms resulted in a rapid recovery in most cases. A very interesting observation in this study was the peeling of the paint from the cold outer wall of this building, apparently attributed to the high NH_3 concentration.

Production of eggs

Although interaction of stress and NH_3 is little known under field conditions, hens' comfort needed for high egg production becomes affected when NH_3 exceeds 20 p.p.m. (14 mg./m.^{3}) (*12*).

Poultry Versus Humans

NH_3 apparently does not constitute a health problem to poultry at levels that are tolerated by the human caretaker. Man could detect NH_3 at the 15 p.p.m. (10 mg./m.^{3}) level, and his eyes would burn at 25 to 35 p.p.m. (17 to 24 mg./m^3). Laying hens were not bothered at the 40 p.p.m. (28 mg./m.^{3}) level, but they began to jerk their heads at the 75 p.p.m. (52 mg./m.^{3}) level (*18, 21*).

Swine

NH_3 toxicity in swine under field conditions is usually associated with other gases (CO_2 and H_2S) and is described in chapters 14 and 25.

Bats

Extremely high NH_3 concentrations (450 to 1,150 p.p.m., or 313 to 800 mg./m.^{3}) in the presence of high humidity in caves where bats inhabit have been responsible for bleaching of bat hair pigment (*9, 20*).

Wild Birds and Mice

Pole-type buildings offer attractive roosting areas for wild birds that represent a perpetual health hazard on farms. Two barns were sealed one evening after the cattle were turned out and filled with anhydrous NH_3 at the rate of 1 pound of gas per 10,000 cubic feet (*11*). After 7 minutes of exposure, the barns were opened; 30 minutes later, the following dead wild birds and mice were removed: 618 starlings, 290 sparrows, 24 mice, and two pigeons; no survivors were found. Then the cattle were allowed to reenter. Since anhydrous NH_3 is harmless to cattle in well-ventilated barns and cost $3 or $4 per 50 pounds, this chemical is very economical in solving wild-bird problems.

EXPOSURE TO NH_3 IN THE LABORATORY

Poultry

NH_3 fumes were produced by the following methods: drip (*23*), sprinkle (*28*), spray (*6*), and gas[1] (*1, 7, 8*).

Immature stock

Symptoms—Keratoconjunctivitis developed in the laboratory when young chickens were exposed to NH_3 fumes[1] (*1, 6, 13, 23, 28*). The levels of NH_3 used in these studies ranged from 0 to 175 p.p.m. (0 to 122 mg./m.^{3}), some at 70° F. and 70 percent relative humidity[1] and others at 18° C. and 21°C. with 50 percent relative humidity (*7*). The incidence of keratoconjunctivitis increased with NH_3 concentration and exposure time; other symptoms included reduced growth at the higher NH_3 levels, unhealthy and unthrifty appearance, and development of "blackfoot" at the 175 p.p.m. (122 mg./m.^{3}) level or at lower NH_3 levels if the litter moisture exceeded 25 percent.

The physiological symptoms revealed (*15*) a significant depression of the hemoglobin content of blood of 4-week-old chicks exposed to 45 p.p.m. (31 mg./m.^{3}) NH_3 for 12 weeks; the presence of an adequate amount of dietary iron indicated that the high NH_3 concentration interfered in some way with the normal utilization of iron in hemoglobin formation.

The pathological symptoms of chickens and turkeys exposed continuously to a low concentration (20 p.p.m., or 14 mg./m.^{3}) of NH_3 were as follows (*1*): No toxic changes were observed until the sixth week of exposure, after which the most notable changes in the respiratory tract were pulmonary edema, congestion, dilation of veins and capillaries, and hemorrhage. No significant differences in weight gains were observed.

Quality of broiler meat.—High NH_3 concentration exerted no adverse effects on the dressing quality of broilers (*18*).[2]

Resistance to disease.—When young Leghorn males 6 to 8 weeks old were exposed to an aerosol of Newcastle disease virus, the infection rate was significantly increased by a 72-hour exposure to 20 p.p.m. (14 mg./m.^{3}) NH_3 or by a 48-hour exposure to 50 p.p.m. (35 mg./m.^{3}) NH_3 (*1*).

Mature stock

Egg production.—Replacement SCWL pullets were exposed to 53 or 78 p.p.m. (37 or 54 mg./m.^{3}) NH_3 from 11 through 46 weeks of age in cages at 19° ± 8° C. and 63 to 65 percent relative humidity (*7*). The 78 p.p.m. level significantly decreased feed consumption from 15 through 30 weeks of age, live-weight gains from 15 to 22 weeks of age, and total egg

[1] SCARBOROUGH, E. N. ENVIRONMENTAL CONSIDERATIONS IN THE DESIGN OF BROILER HOUSES. Paper presented at Summer Meeting Amer. Soc. Agr. Engin. June 24, 1957, 9 pp.

[2] See footnote 1.

production and significantly increased age at sexual maturity by 2 weeks. The only significant detrimental changes on the 53 p.p.m. level were decreased egg production from 23 to 26 weeks of age and increased age at sexual maturity by 1 week.

Layers were exposed to 50 or 100 p.p.m. (35 or 70 mg./m.^{3}) NH_3 at 65° F. for a 10-week period (*12*). Those on the higher level did not lay so well as those exposed to 50 p.p.m. or the unexposed layers. Withdrawal of NH_3 did not permit egg production to return to normal.

Various relative humidity levels (*7*) ranging from 43 to 67 percent were used at two NH_3 concentrations (52 and 104 p.p.m., or 36 and 72 mg./m.^{3}) and at two temperature levels (18° and 28° C.). Detrimental effects on feed consumption, body-weight maintenance, and egg production occurred at the 104 p.p.m. level at 18° C. with 67 percent relative humidity. These detrimental effects did not disappear in the next 12 weeks after NH_3 withdrawal. Similar results were usually obtained at the 28° C. range. In all cases, the 104 p.p.m. NH_3 level produced keratoconjunctivitis by the sixth week of exposure.

Physiological observations (*7*) with hens exposed to 100 p.p.m. NH_3 included: a reduction in the respiration rate by 7 to 24 percent, even if the hens were acclimated to the polluted atmosphere; a a reduction in the CO_2 production and respiratory depth; a slight elevation of the blood pH (6.563 $\pm$ 0.072 vs. 6.447 $\pm$ 0.470 for the controls).

Quality of eggs.—NH_4OH (28 percent NH_3) was added at the rate of 0, 0.05, 0.10, 0.25, 0.50, 1.0, and 2.0 cc. in a 10-inch desiccator; groups of six freshly laid eggs each were exposed to each NH_3 concentration for 14 hours at room temperature and then removed to normal atmosphere for another 32 hours at 50° C. before examination (*10*). The data showed evidence of NH_3 absorption in the eggs and also a significant impairment of interior egg quality as measured by Haugh units, pH, and transmission of light. The conclusions of this study suggested that eggs left all day in the henhouse containing high levels of NH_3 might possibly become affected in quality. Conversely (*8*), exposure of hens to 105 p.p.m. (73 mg./m.^{3}) NH_3 for 10 weeks had no effect on exterior and interior egg quality. Taste-panel studies (*8*) also showed no effect on quality.

Resistance to disease.—Exposure to 20 p.p.m. (14 mg./m.^{3}) NH_3 for 3 days (*12*) increased the infection rate of hens challenged to an aerosol of Newcastle disease virus; however, no increase in infection rate was observed in hens exposed to 30 p.p.m. (21 mg./m.^{3}) NH_3 for 6 days when challenged to a different strain of Newcastle disease virus.

Interactions between NH_3 and nutrition.—A high protein diet supplemented with high levels of vitamins and minerals (*8*) prevented the onset of detrimental effects of NH_3 on egg production, even though feed consumption fell; lowering of the energy content of the diet did not counteract the detrimental effects of high levels of NH_3.

Swine

The only reference (*3*) on NH_3 per se with swine indicated that intraperitoneal injection of NH_4 acetate in doses over 300 mg./lb. body weight was fatal. Before death the symptoms of acute NH_3 toxicosis were rapid respiration, excessive salivation, and clonic-tonic convulsions; no significant gross or microscopic lesions were observed. Toxicosis could also be produced by intravenous fusion of various NH_3 salts. Reduction of proteins in the diet increased the blood NH_3 values when the pigs were intraperitoneally injected with NH_4 acetate. The fact that high levels of NH_3 interfered with the normal utilization of iron in hemoglobin formation in chicks was interpreted (*15*) to suggest that high levels of atmospheric NH_3 in poorly ventilated farrowing houses might be a predisposing factor in the occurrence of iron deficiency anemia in baby pigs.

Cattle

Acute NH_3 toxicity in cattle was produced by adding a water solution of urea directly to the rumen through a permanent fistula (25 g. urea/100 lb. body weight) (*22*). The physiological changes were increased blood NH_3 values, decreased blood pH, increased packed cell volume, loss of water in plasma and red cell solids, frequent defecation, tetonic convulsions, involuntary muscular twitches, and increased respiration. Death was attributed to a metabolic acidosis, because of the high levels of NH_3 ions and their influence on normal metabolic reactions.

Cats, Rabbits, and Guinea Pigs

Cats and rabbits were exposed to 3.5 to 8.7 mg. NH_3/1. (3,500 to 8,700 mg./m.^{3}) of air (average of 7 mg./1.) for 1 hour in a 400-1.-capacity chamber

(*4*). Such exposure increased the output of respiratory tract fluid, the iron content of tracheal, bronchial, and alveolar parts of the respiratory tract, and plasma lipids involving mostly cholesterol fractions. The histological and chemical observations revealed that the naso-bucco-pharynx acted as a partial filter of NH_3, which protected the trachea and bronchi, but not the smaller bronchioles and alveoli, from NH_3.

A species difference in resistance to NH_3 was indicated (*16*): rabbits exposed to 0.48 to 0.53 or 1.47 to 1.52 vol. percent (3,337 to 3,685 or 10,221 to 10,569 mg./m.[3]) NH_3 lived longer in a gas chamber (9 to 53 days) than guinea pigs subjected to the same NH_3 concentrations (4 to 15 days). Also younger animals were more sensitive than older animals of the same species. The principal histopathological changes were lung inflammation, purulent tracheitis, chronic catarrhal and purulent bronchopneumonia, pleuritis, and pericarditis. The conclusions of this study indicated that NH_3 for domestic animals should be lower than 0.25 percent (1,738 mg./m.[3]).

Bats

Experimental exposure of bats to 0.0136 to 0.1166 vol. percent (95 to 811 mg./m.[3]) NH_3 for a total of 52 days (10 hours per day) with a relative humidity of 77 to 92 percent induced a bleaching of bat hair (*9*).

A series of California leaf-nosed bats was exposed to 500 to 5,500 p.p.m. (348 to 3,824 mg./m.[3]) NH_3 for 9 hours (*19*). As the NH_3 concentration increased, the time before death decreased, 40 minutes being required at the 5,500 p.p.m. level. All levels above 3,000 p.p.m. (2,086 mg./m.[3]) were lethal. The data suggested that the bat is much more resistant to NH_3 than man. The physiological changes involved an increase in nonprotein nitrogen from a normal of 38.8 mg./100 ml. to 59.9 mg./100 ml. (388,000 to 599,000 mg./m.[3]), a linear decrease in heart rate from a normal of 600 per minute to death at 5,500 p.p.m. and a decrease in respiratory rate from a normal of 180 per minute to 78 per minute after which it was maintained until death. The pathological conditions attributed to NH_3 toxicity were noted in distinct visceral damage (congestion, distention, hemorrhage), corrosion of the skin and mucous membranes, oily condition of the body hair, skin, and leg membranes, and pulmonary edema.

Pathological findings (*19*) with bats exposed to 3,500 to 5,000 p.p.m. (2,434 to 3,477 mg./m.[3]) NH_3 were similar to those for rats exposed to 1,000 p.p.m. (695 mg./m.[3]) for 12 hours.

Data (*24*) obtained with guano bats experimentally exposed to 3,000 p.p.m. (2086 mg./m.[3]) NH_3 revealed that the guano bat removed 30 to 35 percent of NH_3; this indicates an efficient NH_3 filtering system. The bat also exhaled NH_3 upon its return from highly ammoniated to normal air; the blood pH of 7.66 remained constant during extended exposure to a high concentration of atmospheric NH_3.

RECOMMENDATIONS TO COUNTERACT EFFECTS OF NH_3

Proper management practices and adequate ventilation at the rate of one-half c.f.m. air change per chicken at 4 weeks of age (*17*) to 1 c.f.m. at 8 weeks of age[3] (*18*) should maintain NH_3 concentration at a safe level for poultry.

SUMMARY

Ammonia in the atmosphere at levels tolerated by man (less than 25 p.p.m., or 17 mg./m.[3]) does not constitute an air pollution crisis to domestic animals. Levels not tolerated by man are not commonly present in the atmosphere. These high levels, created by poultry kept under poor management practices, have been known to produce an eye disorder known as keratoconjunctivitis and to affect the overall performance of poultry, especially with high temperature and high relative humidity. Avian leukosis was not influenced by ammonia. High levels of nutrition counteracted the detrimental effects of NH_3; so did proper management and ventilation practices (1 c.f.m. of air change per bird). The physiological and pathological changes were

[3] See footnote 1, p. 15.

restricted to the respiratory tract (pulmonary edema, congestion, hemorrhage, dilation of veins and capillaries, reduced respiration rate and depth) and to changes in the blood pH.

At levels lethal to man, ammonia was not a primary irritant to the guano bat. Bleaching of the hair pigment and an oily condition of the hair, skin, and leg membranes were observed in bats residing in caves containing up to 3,000 p.p.m. (2,086 mg./m.^{3}). Higher levels proved lethal.

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Chapter 6.—Arsenic

Arsenic (As) occurs as an element in coal and other ores and behaves primarily as a nonmetallic agent. In industry, especially copper smelting plants, As is one of the pollutants emitted into the atmosphere. The degree of As deposition on vegetation was dependent on wind and distance (*3, 6, 7, 8, 12, 14, 26*).

With a few exceptions, a majority of As toxicity cases with livestock, as reported in the literature, occurred during the first 40 some years of the 20th century. The biological effects of As poisoning on animals, primarily domestic animals, have been briefly reviewed (*1, 2, 4, 11, 16, 20, 22*). Most of these reviews pertained to ingestion rather than inhalation of As; practically no information could be found on As inhalation under either field or laboratory observations.

EXPOSURE TO As INGESTION IN THE FIELD

Cattle

Symptoms

Arsenic toxicosis was observed in cattle on pasture near smelter plants (*3, 6, 7, 8, 9, 12, 13, 19, 23*). The symptoms occurred mostly in late summer and fall after the completion of vegetation growth (*6, 19, 26*).

The physiological symptoms included inflamed eyes and mucous membranes of the upper air passages, runny noses, diarrhea, thirst, emaciation, excessive salivation, incoordination of gait, breath of garlic odor, and rough coat. The pathological symptoms revealed inflammation of the gastrointestinal tract, fatty degeneration of stomach and kidney glands, muscular atrophy, congestion, hemorrhage, and proliferation of connective tissue cells of organs, particularly kidneys. (*6, 7, 8, 19*)

In one case, the acute As intoxications included vomiting, diarrhea, gastric mucosa damage, and fatty degeneration of liver; whereas, the chronic symptoms involved increasing cachexia, eczema, and muscular paralysis (*13*). Presence of As caused peptic ulcers in cattle (*23*).

Production and quality of milk and beef

Milk yield was lowered as much as 12.5 percent among affected cattle grazing near As emitting smelters (*6, 9*). Milk fat was reduced by 8 percent (*9*). Beef production was decreased because of abortions and lowered weight increases (*19*).

Reproduction

Abortions and failure to breed were greater in polluted than nonpolluted areas (*6, 9*).

Content of As in milk, beef, and organs

Milk of cows exposed to areas that averaged 0, 10, and 33 kg. As/km.^{2} in the dustfall per year contained an average of 0, 7.7, and 12.5 mcg. percent As (on a dry basis), respectively (*12*). The spleens, kidneys, and loins of bulls and cows exhibited an As content of 2.4 to 9.3 mg./kg., when exposed to contaminated pasture containing 3 to 227 mg./kg. dry weight (*3*).

Tolerance levels

A maximum permissible concentration of 0.17 mg./m.^{3} of AsH_3 was recommended for cattle exposed to As-contaminated areas (*21*).

Horses

Numerous poisoned horses along with cows and sheep were found scattered all over about 100 square miles of the territory surrounding the Anaconda smelter in November 1902 (*6*). The symptoms were: raised red line at the base of incisor teeth, breath of garlic odor, falling of hair, ulcers of nose, imperceptibility of pulse, erosions on outer side of gums, puffiness above eye, rough hair, partial paralysis of hind limbs; difficult breathing, increased heart beat, dilation of pupils, partial paralysis of diaphragm, and costal breathing. The As content was highest in nose ulcers (658 p.p.m.) and lowest in fluids (0.03 p.p.m. in blood); both urine and tail hair contained 58 to 59 p.p.m.

In 1965, 16 horses and eight asses were found with symptoms of As poisoning in Pola de Lena, Spain (*19*). The acute symptoms were cerebral involvement and signs of intense pain with head banging.

Chronic symptoms included diarrhea, colic, weakness, muscular aches and twitches, paresis, hard skin, cachexia, and paraplegia. Sudden death occurred in many cases.

Sheep

Sheep were found dead among cattle and horses in November 1902 near an Anaconda smelter. Although symptoms were given for cattle and horses, none were described for sheep (*6*).

Honey Bees

Bees were very sensitive to the presence of As on pollen as a result of atmospheric As deposition (*2, 3, 5, 14, 24, 25*). The As content of healthy and poisoned dead bees ranged from 0.0 to 0.091 and from 0.072 to 0.624 mcg. per body, respectively (*5*). Within a 6 km. radius of the electricity-producing plant where As was discharged into the air, 452 bee colonies were destroyed and 171 colonies too weakened to be of any value. At distances of 300 m. to 5 km. from the electric plant, the As content stored in pollen was 0.0001 to 0.0017 percent; if the toxic dose of As per bee were 0.5 mcg., the daily rate of 300 mg. pollen would expose the bees to 0.3 to 5.1 mg. As (*24*).

Wildlife

Peculiar skin and hair injuries were observed in red deer and hares (*17, 23*). The symptoms included loss of hair in spots or over the entire body with a blackened skin, scleroderma, alopecia, inflamed respiratory and digestive tracts, gelatinous infiltration with noticeable thickening of the connective tissue, an occasional case of liver cirrhosis and endemic paresis, and antler malformation. The red deer were more affected than hares. Laboratory analysis indicated As poisoning.

TOLERANCE STUDIES

The fatal dose for horses and cows was 300 grains of As per day, as contrasted with 4 to 8 grains for sheep. Horses and cattle could ingest 20 to 30 grains of As daily continuously with no apparent ill effects (*18*). The lethal dose of As varied between individuals among horses. Although the usual lethal dose ranged between 10 and 15 grams, some died on 3 grams and some survived on 30 grams (*27*).

Animals that had been exposed to the As contaminated areas for some time outlived those animals shipped into the same areas (*6*).

MISCELLANEOUS

Although not relevant to air pollution, the following study (*15*) with rabbits injected with 3 to 5 cc. of 1 percent potassium arsenate solution deserves consideration from the physiological viewpoint. Muscular cramps resulted shortly after injection, and death occurred in 6 to 37 hours. Phosphoric acid levels were reduced, as well as hexose monophosphate esters, hexose monophosphoric acid, and adenylpyrophosphoric acid. The hypothesis proposed that acute As poisoning affected the phosphorylation of muscle cells, which would explain muscular cramps, followed by a detrimental effect on the contractile elements of the capillaries.

In view of the atmospheric As contamination on vegetation and the resultant toxicity in livestock, farmers were concerned about their grains (barley, wheat, oats) being dried by flue gas from coke containing from 0 to 80 p.p.m. As. However, in no instance did the dried grain contain more than 0.2 p.p.m. As (as As_2O_3); hence, slight, if any, contamination should result from the flue gas method of drying (*10*).

RECOMMENDATIONS TO COUNTERACT EFFECTS OF As

Removal of As from the powerplant emissions was strongly recommended (*3*). Change of location of grazing pasture was another one, in which 80 percent of the 125 cases studied showed some improvement (*19*). The use of $Fe(OH)_2$ solution to decrease the poisonous effects of As compounds was recommended (*25*). In other cases, especially with chronic As poisoning, complete recovery was not possible because of permanent damages (*18*).

SUMMARY

Of the animals studied in the field, honey bees are the most susceptible to arsenic toxicosis; sheep are next most susceptible. Horses and cows apparently are the most resistant; 300 grains of As daily proved fatal for horses and cows, as contrasted with four to eight grains for sheep. Wild animals (red deer and hares) were reported to have suffered from As poisoning.

The physiological and pathological findings in As poisoned animals via ingestion of contaminated vegetation included inflammation of respiratory and gastrointestinal tracts, runny noses, diarrhea, incoordination of gait, muscular atrophy, breath of garlic odor, rough coat, nose ulcers, and raised red line at the base of incisor teeth of horses, skin lesions, falling of hair, fatty degeneration of certain organs in the body, hemorrhage, proliferation of connective tissue cells of kidneys and other organs, and congestion. Death occurred in many cases.

No information could be found on effect of As inhalation on animals.

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Chapter 7.—Beryllium

Beryllium (Be), a rare element, is becoming increasingly important as it is a constituent of rocket exhaust products. Much of the work with Be was done with laboratory animals in the early 1950's. Some of this work will be discussed in this chapter to supplement the meager knowledge of Be toxicosis in farm animals. All the references herein pertain to inhalation of Be fumes and dust in the laboratory; one of these references also included results with the ingestion and injection methods.

DOGS

Two young adult beagles were exposed for 20 minutes to rocket exhaust products containing a mixture of Be compounds at an average concentration of 115 mg./m.^{3} (*4*). Lethargy was the only symptom observed the first few days after exposure, after which the dogs became normal for the 3-year period of the study. After sacrifice of the dogs, the lung tissue was examined electron microscopically and was found to contain Be particles and agglomerates less than 1μ in size, mostly in the cytoplasm of histiocytes in the interstitium of the septa. The lesions were more typical of the classical reaction to a foreign body than immunologic in character and represented an early form of chronic Be disease that may be paralleled in the human disease.

DOGS AND OTHER ANIMALS

Tolerance Levels

The 48-hour minimum lethal dosage for Be metal dust and insoluble Be compounds was greater than 100 mg./kg. of rat; that of the soluble Be compounds BeF_2, $BeSO_4$, and Be oxyfluoride was 15, 10, and 2 mg./kg. of rat, respectively (*3*). Guinea pigs given 90 exposures in a 107-day period to 189 mg. Be/m.^{3} as a Be dust resulted in 44 percent mortality, as contrasted with no mortality for those given 33 exposures in a 39-day period to 233 mg. Be/m.^{3}; 100 percent mortality occurred within 90 minutes in other guinea pigs exposed to a combination of Be dust and BeF_2 (*2*). Daily inhalation of $BeSO_4$ mist (9 mg./m.^{3} per 6 hours per day repeated five times per week for a month) was toxic in all cases to rats, but alternate daily exposure was not toxic (*5*). The lethal levels of $BeSO_4.6\ H_2O$, mist and length of exposure, were: 100 mg./m.^{3} (14 days + 66 hours) and 50 mg./m.^{3} (51 days + 234 hours) for rat, hamster, guinea pigs, dog, cat, goat, pig, monkey, and chicken; 10 mg./m.^{3} (95 days + 426 hours) for cat and rat; and 1 mg./m.^{3} (100 days + 426 hours) for none of the animals studied, including the rabbit and mouse (*7*). The data obtained with the chicken, pig, and goat were insufficient to warrant valid conclusions on Be toxicosis of these animals.

Symptoms

The symptoms of Be toxicosis via inhalation have been defined (*2*). The acute symptoms were labored breathing, coughing, irritation to eyes and nasal passages, convulsions, and death. The chronic symptoms included weight changes, histologic pulmonary damage, anemia, changes in arterial O_2 tension, and changes in N metabolism. The severest and most extensive lesions occurred in the lungs of dogs, intermediate in cats and rabbits, and minimal in rats (*1, 6, 7*). Prolonged exposure of rats to Be resulted in two basic changes in lung tissue: inflammatory (histiocytes, cellular lesions, thickening of alveolar walls, collangenous, and fibrotic changes) and neoplastic (epithelial proliferation after 6 months of inhalation and cancer after 9 months of inhalation) (*8*). These inflammatory and neoplastic changes were responsible for Be pneumonitis that resembled that in humans; the Be compounds were specific in reactions with enzymes (some Be compounds were inhibited, unaffected, or activated) and were found to alter the RNA distribution but not DNA and lipids. One study (*2*) indicated that Be poisoning induced Be-rickets in guinea pigs, but the evidence was insufficient.

Be Distribution

In guinea pigs exposed to Be dust inhalation, Be deposition was most concentrated in the lungs (*2*). Exposure to BeF_2 resulted in deposition of Be in lungs, pulmonary lymph nodes, liver, skeleton, and bone marrow of dogs; the rate of deposition in the lungs and pulmonary lymph nodes increased with duration of exposure (*1, 6*). If the Be content of the femur was used as representative, deposition was greater in the skeleton than in any other tissue examined with the exception of lungs and pulmonary lymph nodes in rabbits, cats, dogs, and rats but not in guinea pigs or mice.

Comparison of Be Compounds

Soluble Be compounds (BeF_2, $BeSO_4$) were more toxic than insoluble Be compounds (BeO) or Be metal dust, because of hydrolysis and of mechanical interference with normal lung function rather than by any specific toxic effect of Be per se; acute toxicity was associated with soluble Be salts and chronic toxicity with insoluble Be salts (*2, 3*).

Of the soluble Be compounds, BeF_2 was more toxic than $BeSO_4$ (*1, 3, 5, 6*). Animals exposed to Be via inhalation, intraperitoneal injection, and oral administration showed that Be itself is not toxic (*2*).

In relation to the Be content in lungs, a considerably greater proportion was distributed to the skeleton, liver, spleen, and kidneys of dogs exposed to BeF_2 inhalation than to BeO or $BeSO_4$ mist (*1, 6*).

Alleviators

Daily administration of a dietary supplement of "Lextron" failed to prevent the development of Be anemia in dogs (*1*). Vitamin B_{12} was of little prophylactic or therapeutic value in controlling the anemia syndrome (*1, 6*).

SUMMARY

Research with laboratory animals, including dogs, cats, and rabbits, indicated that soluble Be compounds were more toxic than insoluble Be compounds and that acute and chronic Be toxicosis were associated with soluble and insoluble Be salts, respectively. Of the soluble Be salts, BeF_2 was more toxic than $BeSO_4$. The pathological symptoms of Be toxicosis were primarily restricted to pulmonary damages, body weight changes, and anemia. The physiological symptoms included specificity of Be compounds in reactions with enzymes and alteration of the RNA but not DNA and lipids. Be deposition, for the most part, was greatest in lungs and pulmonary lymph nodes; the rate and quantity of deposition depended on the solubility of the Be compound.

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Chapter 8.—Cadmium

Cadmium (Cd) has been in great demand by the automobile industry for Cd-plated nuts, bolts, and other small parts and for Cd-nickel and Cd-silver alloys as bearing metals. A signficant correlation was observed between atmospheric Cd and heart diseases in humans (*2*). No information could be found in the literature survey about atmospheric Cd and its effects on domestic animals. Excerpts on Cd research with animals in the laboratory are included herein to give a better perspective of Cd toxicosis that might occur naturally among domestic animals.

EXPOSURE TO Cd INHALATION IN THE LABORATORY

Rabbits, Goats, and Rats

Rabbits, goats, and rats were exposed in a 10m.^{3} chamber to CdO or $CdCl_2$ fumes in doses up to 1,000 min. mg./m.^{3} (*10*). (The min. mg./m.^{3} refers to length of exposure in minutes × concentration of fumes.) The length of exposure was not mentioned for rabbits and goats but for rats in a few cases. The pathological findings were confined to the lungs and varied with the period of survival. Three clearly defined stages were observed: (a) acute pulmonary edema developing with 24 hours of exposure and reaching its peak within 3 days, (b) proliferative interstitial pneumonities, which lasted from third to 10th day after exposure, and (c) permanent lung damage in the form of perivascular and peribronchial fibrosis. Further studies with rats proved that repeated small inhalation doses of Cd fumes were noncarcinogenic; 125 min. mg./m.^{3} was tolerated, but 250 min. mg./m.^{3} produced permanent lung damage.

Dogs

The LC_{90} for dogs exposed to atomized aqueous $CdCl_2$ solutions was 0.32 mg. Cd/l. (320 mg./m.^{3}) air for 30 minutes (*3*). The physiological symptoms were: salivation, occasional vomiting, bradycardia, and rapid respiration of the asthmatic type. About 50 percent of the fatalities occurred within the first 24 hours after exposure. The pathological changes included pulmonary edema, necrosis of respiratory bronchiole epithelium lining, emphysema, and scarring in later stages. Tissue analyses showed that a considerable proportion of inhaled $CdCl_2$ left the lungs and was distributed throughout the body, with the greatest amount being deposited in the kidneys. The fraction left in the lungs became fixed and persisted for at least 15 weeks.

Rats

Exposure of rats to Cd aerosols at various concentrations disturbed the conditioned reflex activity without manifestations of changes in the general condition or behavior (*5*, *6*). Intermittent exposure to 3 g./1. (300 g./m.^{3}) for 2 hours every 2 weeks produced enlarged, rigid lungs with less air per gram of lung tissue (loss of compliance); the histologic changes represented variability of aveolar size, thicker aveolar septae, and an increase in the interstitium (*13*).

EXPOSURE TO Cd INGESTION IN THE LABORATORY

Cattle

Three Holstein cows were each given 3 grams of Cd by capsules daily for 2 weeks (*7*). Feed consumption dropped sharply after initial ingestion of Cd but returned to normal during the second week. Milk production declined rapidly for several days and then increased to an intermediate level. After cessation of Cd administration, the milk yield increased by 50 percent. Body weight loss occurred; no other clinical manifestations of Cd toxicity were observed. Analysis of feces and milk indicated that 82 percent and less than 0.022 percent of the ingested Cd were excreted via feces and milk, respectively.

Swine

A ration containing a wormer (0.044 percent Cd anthranilate) was fed to shotes in dry lot (*1*). Deaths occurred: autopsy revealed anemia, enlarged spleen, numerous linear ulcerations of stomach, enlarged mulberry-shaped heart, marked fatty degeneration of liver and kidneys, and icteric skin. Withdrawal of medicated feed eliminated the symptoms of Cd toxicity.

Rats and Mice

Both rats and mice fed a "Cd-free" diet (*11, 12*) did not differ with respect to growth and general health from those fed the same diet plus 5 p.p.m. Cd as a soluble salt in the drinking water. However, the Cd-exposed animals, especially males, had a higher mortality rate than the controls.

EXPOSURE TO Cd INJECTION IN THE LABORATORY

Although not relevant to atmospheric Cd toxicosis, the following data should be of interest from the physiological standpoint:

Pigeons

An intramuscular injection of $CdCl_2$ (0.2 ml. of a 0.04 M solution) (*4*) did not produce necrosis of the seminiferous tubules of wood and feral pigeons; however, an intratesticular injection of $CdCl_2$ (0.1 ml. of a 0.04 M solution) did produce localized necrotic damage and a great disruption of germ cell coordination in the seminiferous epithelium of both species of pigeons.

Laboratory Animals and Rabbits

Subcutaneous injection of $CdCl_2$ (0.04 millimole/kg. body weight) in rats, mice, hamsters, and rabbits (*9*) resulted in necrosis of the testes but not other organs. Females were not affected as shown by fertilization and birth of young. Hence, the Cd effect was specific for the male gonad only.

ALLEVIATORS

Treatment with different levels of BAL (2, 3 dimercaptopropanal) via injection (*3*) reduced the mortality of dogs exposed to Cd inhalation to about 50 percent of that of the untreated exposed dogs; large doses were necessary when administered as soon as possible after exposure but not continued beyond the first day.

Cd toxicosis of the male gonad of rats, mice, rabbits, and hamsters was counteracted largely by Zn at the rate of 4.8 millimole Zn acetate/kg. body weight (*9*).

MISCELLANEOUS

The paucity of literature on Cd in milk production led to the investigation of this problem (*8*). Market milk samples were collected on a quarterly basis from 61 cities throughout the United States. These 61 cities represented two areas: 20 in area 1 (Southeast) and 41 in area 2 (Northeast and Southwest). The average Cd content of milk from both areas varied between 0.017 and 0.030 p.p.m. Significant differences in Cd content from one sampling period to another were noted. Milk from all States except the Southeastern States showed significant differences between cities. Analysis of 32 milk samples from individual cows showed Cd variations from 0.020 to 0.037 p.p.m., with an average of 0.026 p.p.m. For man, the established safe level for Cd in drinking water is 0.01 p.p.m. and the toxic level is 3 mg.

SUMMARY

Cadmium toxicity symptoms varied with the type of exposure: (a) inhalation produced primary pulmonary disorders in rats, rabbits, dogs, and goats; (b) ingestion resulted in higher mortality in rats and mice, more so in males than females, when given Cd in the drinking water; inflammation of gastric tract, degeneration of liver and kidneys, anemia, enlarged spleen, and enlarged heart in swine,

when given Cd in the feed; and reduced body weights and milk production in cows, when given Cd in capsules; and (c) injection induced necrosis of the testes of rats, mice, hamsters, rabbits, and pigeons and was specific for the male gonad only. Zn and BAL (2, 3 dimercaptopropanal) were partially effective in counteracting the toxic effects of Cd in the male gonad of laboratory animals and in dogs exposed to Cd inhalation, respectively.

The fact that the Cd content of market milk samples was higher in some cases than the safe limit of 0.01 p.p.m. in the drinking water for man deserves some consideration, because the sources of Cd contamination of market milk were either unknown or not reported.

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Chapter 9.—Carbon Monoxide

Carbon monoxide (CO) is an active poisonous gas that combines with the hemoglobin of the blood corpuscles to form a stable compound; thus this compound prevents the absorption of oxygen by the blood. Sources of this gas are incomplete combustion from tobacco smoking, automobile engines, mine shafts, interior of warships during a battle, volcanoes, fires, metallurgical industries, and others. Comprehensive reviews on CO poisoning were devoted mostly to humans and laboratory animals (*9, 11, 13, 30*).

EXPOSURE TO CO IN THE FIELD

Several field cases of CO poisoning were reported for cats (*7*), dogs (*7, 8, 29*), cattle and swine (*12*), horses (*23*), and chickens (*3, 25*). The physiological symptoms included deafness and lethargy in cats and dogs, and excitation and strongly projected mucous membranes in horses. Sudden deaths in cattle, swine and chickens have been observed. The pathological findings revealed cherry-red lungs, greatly dilated bronchi, and large amounts of CO in the blood. The meat of CO poisoned cattle and swine was considered edible.

EXPOSURE TO CO IN THE LABORATORY

Dogs

Acute CO symptoms

When dogs were exposed to 0.05 to 1 percent (573 to 11,452 mg./m.^{3}) CO gas for 60 minutes or 2.5 percent (28,630 mg./m.^{3}) CO for 15 minutes (*28*), the heart excitability was lowered not only during gas inhalation but also became more severe after cessation of gas inhalation. The disturbances of heart muscles may be attributed to disturbances of myoglobin or cytochrome C or both.

The hemodynamic alterations observed (*22*) in dogs during inhalation of 0.8 to 2 percent (9,162 to 22,904 mg./m.^{3}) CO were an increase in cardiac frequency, a slight increase in the systemic pressure, and a twofold or threefold increase in pulmonary artery pressure. The data suggested that the pathogenesis of chronic pulmonary heart was not caused by the decreased alveolar O_2 tension so much as to the lessened O_2 content of the blood.

Dogs were given a mixture of coal gas and air with a concentration of 0.37 percent (4,237 mg./m.^{3}) CO to breathe until the carboxyhemolglobin (COHb) level reached 70 percent (*20*). The time taken to reach 70 percent saturation with COHb was 107 to 169, 97 to 144, and 96 to 185 minutes, respectively, for the first, second, and third separate gassing occasions. The time taken to reach apnea was 87 to 110 and 120 to 270 minutes, respectively, for rapid gassing and slow gassing, the COHb level was 70.5 and 69 percent, respectively. Respiratory alkalosis occurred from hyperventilation caused by metabolic acidosis (rising levels of lactate and fall in bicarbonate level); in the latter stage of gassing, when respiratory depression occurred, the P_{CO_2} returned to normal values. No evidence of respiratory acidosis (CO_2 retention) in blood was observed even at the point of apnea.

Chronic CO symptoms

Dogs exposed for $5\frac{1}{2}$ hours per day, 6 days per week for 11 weeks to 0.01 vol. percent (115 mg./m.^{3}) CO and reaching daily 20.1 $\pm$ 1.1 percent COHb (*18*) showed a consistent disturbance of postural and position reflexes and of gait; some dogs showed a pathological electrocardiogram characteristic of anoxia and necrosis of single heart muscle fibers. Three months after termination of the study, the central nervous systems revealed histologic changes in the cortex and white matter of the cerebral hemispheres and in the globus pallidus, and the brain stem; these alterations corresponded in type and localization to those found in acute CO poisoning, but they were smaller, more scattered, and less destructive.

A group of seven dogs (*31*) was given a daily 6- to 8-hour exposure to 0.08 percent (916 mg./m.^{3}) CO for 20 weeks and then 0.10 percent (1,145 mg./m.^{3}) for the next 16 weeks; their tolerance to CO was compared with that of normal dogs, CO-acclimatized dogs, altitude-acclimatized dogs, and dogs transfused with blood from normal dogs. The data showed an increased tolerance to CO: (a) The rate of CO uptake appeared to be independent of the O_2 (or CO) capacity of the blood; hence, those animals with a lower capacity (normal dogs) would undergo a more rapid use in saturation percentage than acclimatized dogs having a higher capacity. (b) Since the acclimatized and normal dogs exhibited the same COHb percent in the steady state at sublethal concentrations, the acclimatized dogs would have more Hb available for O_2 combination when the steady state was reached because they have a greater hemoglobin level. Other data (*31*) showed (a) no evidence of factors, other than hematologic, that increased the tolerance of dogs to CO and (b) increased tolerance of dogs subjected to altitude or transfused with blood from normal dogs, similar to that accomplished by chronic exposure to low CO levels.

CO and alcohol

Dogs were exposed to 0.01 percent (115 mg./m.^{3}) CO for 6 hours per day, 5 days per week for 21 weeks and given 15 percent ethyl alcohol in drinking water and 60 ml. of 15 percent alcohol by stomach tube just before CO exposure and 3 hours later during exposure (*21*). The data revealed no significant summating effects of CO and alcohol from a physiologic standpoint (Hb, COHb, blood alcohol values, body temperature) as compared with controls given neither CO nor alcohol or those given one or the other.

Resistance to disease

The immunological potency as a result of vaccination with streptococcal vaccine was lower in dogs exposed to 1 percent (11,452 mg./m.^{3}) CO for 4 hours per day for 40 days than in nonexposed dogs or nonvaccinated exposed dogs, probably because of the alteration of plasma protein composition caused by CO intoxication (*1*).

Alleviators

The chief objective in reversing CO poisoning is the restoration of an adequate O_2 supply to the heart and brain. Of the three gases used in resuscitation—carbogen (combination of CO_2 and oxygen), 100 percent O_2, and air—carbogen was most effective in eliminating CO from the blood (*10, 14, 15, 24*). The type of carbogen used was either 7 percent CO_2 + 93 percent O_2 or 5 percent CO_2 + 95 percent O_2. In one study 7 percent carbogen cleared the blood of CO more rapidly than did 5 percent carbogen but not so in another study. The differences were attributed to a different respiratory valve used in resuscitation (*10*). However, 7 percent carbogen was preferred to 5 percent carbogen for human resuscitation (*19*).

During the first hour of recovery, approximately 60 percent of the CO lost from the blood appeared in the expired air of dogs resuscitated with 5 percent carbogen, as contrasted with 43 percent for those breathing air. The blood pH gradually rose to normal levels while the blood lactate fell during recovery (*14*).

Chickens

Toxicity levels

In young chickens 1 to 42 days of age (*6*), 160 p.p.m. (183 mg./m.^{3}) CO produced no ill effects as long as 7 days, 600 p.p.m. (687 mg./m.^{3}) CO produced distress after 30 minutes of exposure, and 2,000 and 3,600 p.p.m. (2,209 and 4,123 mg./m.^{3}) CO produced death after 2 hours and 30 minutes of exposure, respectively. The COHb levels ranged from 7 to 12, 25 to 50, 63 to 75, and 63 to 75 percent, respectively, for the 160, 600, 2,000, and 3,600 p.p.m. levels. Those chickens exposed to 600 p.p.m. (687 mg./m.^{3}) CO recovered rapidly when placed in a normal environment.

Experimental gassing of 30 chicks with 0.4 percent (4,581 mg./m.^{3}) CO, with the CO_2 removed, produced the first death in 79 minutes and another 21 deaths by 162 minutes; the eight survivors recovered when transferred to fresh air but became unthrifty and died later. Exposure to 0.8 percent (9,162 mg./m.^{3}) CO, in presence of CO_2, caused death within 60 minutes to 22 out of 30 3-week-old chicks, all three pigeons, all six adult guinea pigs, but not the one rabbit under study; five 2-week-old poults given 0.8 percent CO, with the CO_2 removed, died within a few days. Hence, tolerance to CO appeared to be greater in the absence than in the presence of CO_2 (*26, 27*).

Symptoms

The chief symptoms of acute CO poisoning were (*6, 26, 27*): irritability, drowsiness, incoordination of gait, dyspnea, anoxemia, toe and wingtip picking, head shaking, and clonic spasm; those of subacute CO poisoning included impaired appetite, unthriftness, chillness, retarded development, and coma. The pathological symptoms were cherry-red color in all tissues, particularly lungs, and presence of CO in the blood. These pathological symptoms, however, were not observed (*3*) in 12-week-old chickens that died in 20 seconds from experimental CO gassing by means of the automobile exhaust pipe. Autopsy 4 hours later revealed a dry, whitish breast muscle typical of muscle fixed in a weak formalin solution and small amounts of bright-red clotted material in the thoracic cavity; neither lungs nor the blood showed any deviation from normal.

The histopathological lesions included (*6*) dilation of brain blood vessels with stasis of red blood cells, perivasular and perineuronal edema, degeneration of neuronal cells of the strial area, and degeneration of the Purkinje cells of the cerebellum. These histopathological lesions should not be considered as specific for CO poisoning, because they are observed in a number of other diseases afflicting the central nervous system.

Rabbits

A direct relation between ambient temperature and CO toxicity was demonstrated (*17*) with rabbits exposed to 0.1, 0.2, or 0.4 mg. CO/1. (100, 200, or 400 mg./m.^{3}) at three temperature ranges (20°–25°, 30°–35°, 40°–45° C.). The CO toxic symptoms especially at high ambient temperature were: depression, motionlessness, convulsions, rapid respiration, loss of body weight, and increase in erythrocytes, COHb values, and blood viscosity. Also, a disturbance of the thermoregulatory process occurred as a result of the rabbit's resistance to temperature being reduced; thereby, a synergism between CO toxicity and hyperthermy is produced.

The physiological responses of rabbits exposed to CO and air indicated (*16*) a relationship between COHb values and activity of the animal. When the COHb values reached 35 percent in 40 minutes and 55 percent in 80 minutes, the rabbits assumed a normal sitting position and a lying position, respectively. Meanwhile, the electrocardiogram patterns showed a change from fast waves to slow waves with spindle bursts. After CO withdrawal, the rabbits resumed the normal sitting position 10 minutes later; and when the COHb value decreased to 45 percent, the EEG pattern was reversed.

Exposure to CO (0.017 percent (195 mg./m.^{3}) followed by 0.035 percent (401 mg./m.^{3}) for a 10-week period appeared (*2*) to intensify the development of atheromatosis in rabbits fed 2 percent cholesterol but not in noncholesterol-fed rabbits. The symptoms characteristic of atheromatosis included degenerative changes in the heart, scattered hemorrhages, and pronounced vascular changes. The differences between cholesterol-fed and control rabbits might be explanined by tissue hypoxia due to a CO-induced displacement of the O_2 dissociation curves to the left, in combination with a decreased activity of certain enzymes inhibited by CO.

Species Differences

Species susceptibility to CO poisoning occurred in the following decreasing order: canary, mouse, chicken, small dog, pigeon, English sparrow, guinea pig, and rabbit (*5*).

Chronic CO intoxication occurred in dogs at CO concentrations that have been regarded as being within the safety limits for man (*18*).

In one study (*4*) an investigator took canaries and pigeons with him to a gastight 80-cubic-foot chamber containing 0.25 percent (2,863 mg./m.^{3}) CO. The canaries showed distress in 1 minute and fell from perches in 3 minutes; the pigeons showed slight distress in 11 minutes; the investigator himself suffered a slight headache in 20 minutes at the end of the test, after which he became ill for several hours.

SUMMARY

Several discrepancies have been found in the literature survey about the description of physiological and pathological symptoms of carbon monoxide (CO) poisoning occurring in the field and in the laboratory. Some of the reasons that might account for the discrepancies may be differences in temperature, quantity and type of gases present with CO, dietary regime, and degree of previous exposure to CO in low concentrations (acclimatization).

Domestic animals vary in their susceptibility to

CO toxicity. The physiological symptoms included sudden deaths of large numbers of animals, temporary or permanent deafness in cats and dogs, drowsiness, incoordination of gait, dyspnea, coma, and clonic spasm. The pathological symptoms for the most part revealed a cherry-red color in all tissues, inflamed respiratory tract, high CO levels in the blood, altered EEG patterns with rabbits and ECG patterns with dogs, changes in the central nervous system in the brain region of dogs, hypertrophy of the heart and hemodynamic alterations in the dog, and a synergism between CO and hyperthemy in the rabbit and between CO and CO_2 in poultry.

Presence of alcohol or vaccination with a streptococcal vaccine did not produce any additive effects with CO. Five or seven percent carbogen was a much more effective alleviator than 100 percent of O_2 or air in eliminating the CO from the blood during resuscitation. The meat of CO-poisoned cattle and swine was considered edible.

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Chapter 10.—Dusts

The term "dust" is best defined as particles floating in the air. These particles are chiefly solid bodies and are composed of salts, minerals, and soil, of soot and other particles of unburnt fuel, of bits of hay, straw, weeds, and other debris of plants, of fragments of insects and other debris of animals such as feathers, skin, and hide hairs, and of living particles such as bacteria and plant spores. Some of the airborne bacteria are pathogenic to animals and plants; plant spores can produce putrefaction of foods (molds). Although excess dust can be harmful to life, dust particles are necessary in the atmosphere for formation of clouds to produce rain.

Since little was known about the bulk density or specific density of particulates in urban atmospheres, air samples were obtained from the Pittsburgh, Pa., area for analysis. The bulk densities and specific densities of the air samples were 0.49 to 0.64 and 2.0 to 2.6 g./cm.^{3}, respectively. These data provide some basis for explanation of unpredictable responses reported after inhalation of mixtures of pollutant gases and particles by animals and man (*13*). The amount and nature of particulates in the air were influenced by weather (dry vs. damp), season (less insect fragments in cold weather), wind, species and activity of animal, housing, and sampling location (*11, 12, 16*). In various animal lodgings, the dust particle size under normal conditions averaged from 60 to 80 motes (small particles in 1 cc. of air (*10*). During activity such as feeding of animals, the dust particle size increased to more than 500 motes in 1 cc. of air. The greatest quantity of motes was below 1 micron. Since motes up to 5μ in size are capable of entering the remote parts of the respiratory tract, the necessity of further investigations in atmospheric dust seemed to be well-grounded. Electron-microscope studies (*14*) of asbestosis in man and animals revealed pathogenesis within the respiratory tract of small dust particles less than 1μ in length. Consequently, the havoc created by duststorms of the Midwest in the 1930's should have affected the health of farm animals. However, the only information found in the literature survey referred to waterfowl, several species of flying birds, and small animals.

The biological effects of atmospheric dusts have been briefly reviewed (*3, 42*). Many of the specific contaminants in dusts (metal oxide dusts, mineral dusts, and others) are described either in this chapter or in other chapters. An unidentified inorganic trace factor found in atmospheric dust was essential for normal health status of rats fed an amino acid basal diet in a controlled environment (ch. 2, p.3.)

EXPOSURE TO DUST INHALATION IN THE FIELD

Cattle

General

One hypothesis (*5*) for the high fatalities in cattle and men during the Belgian fog of 1930 was the presence of poisonous ricin dust being blown from French Morocco in the duststorms. This ricin dust, which came from castorbean cake used as a fertilizer, probably accumulated in the dense fog and precipitated anaphylaxis in cattle and in man.

A "fog fever" syndrome (*30*) occurs in Great Britain among cattle being kept in total confinement where they are exposed to atmospheric dusts and molds. The symptoms of fog fever are very similar to those of emphysema in the United States. Death is not common.

Quality of milk

If the feeding and cleaning jobs are done at least 2 hours before milking (*46*), the dust concentration in the barn will be reduced to a minimum so that the milk will remain relatively uncontaminated. Sanitation around creameries was stressed (*11*) because 11.1 percent of the 150 air-sample analyses indicated the presence of feather parts; 15.2 percent, rodent-type hairs; 26.3 percent, other types of hairs; 35.3 percent, insect parts; 58.2 percent, vegetable matter; 63.8 percent, cloth fibers; 63.2 percent, sand and clay; 67.3 percent, coal dust: and 76.5 percent, unidentified particles.

Dogs and Rabbits

Some studies (*40*) on the inhalation of coal dust by dogs and rabbits were conducted as early as 1878. The results showed that soot from dry coal was less harmful to the respiratory tract of dogs and rabbits than various forms of mineral dusts or even dry coal soot suspended in a liquid.

Horses

Analysis (*18, 19, 20*) of dust deposited in the lungs of horses exposed to years of underground work in coal mines showed that the dust retention was significantly lower than in human beings with comparable exposure time, probably because the horses were used in locations with lower dust concentration. The dust content per gram of dry tissue was higher in the well-ventilated than in the poorly ventilated parts of the lungs of the horses; on the basis of dry weights of organs, the lymph glands contained four times as much dust as the lungs. The dust distribution in the lungs of the horses, its particle-size distribution, and the chemical composition differed considerably from those values in human beings. Since no titanium or aluminum was found in horse lungs and since the total and free silicon oxides were substantially lower than in human beings, the data on dust retention in horses could not be applied to human workers.

Poultry

Dust origin and composition

Poultry dust originates from feather and skin debris, feed, and litter. The quantity of dust produced in poultry houses varies with the type of litter used and increases with age of litter and at certain temperatures (60° to 70° F.) (*23, 24, 25, 27*). Dust production is inversely proportional to the relative humidity, is less in cages than on litter, is greater during periods of illumination than of darkness, and is greatly reduced when broilers reach the seventh week of age. The chemical analysis of poultry dust revealed 92 percent dry matter, 60 percent crude protein, 9 percent fat, and 4 percent fiber. On a dry basis, broiler dust contained lower fat and higher protein values than hen dust. This analysis was verified by another investigator (*6*).

Performance

In studies (*23, 24, 25, 27*) on dust origin and composition in poultry houses, where broilers and layers were maintained on litter or in cages, no data were submitted to determine the effect of poultry dust on the overall performance of the birds. Broiler performance (*44*) was far superior in dust-free pens than under field conditions, probably because of the presence of airborne diseases affecting the respiratory tracts of birds in the field. The presence of airborne diseases was observed (*15*) in even emptied, cleaned, and disinfected poultry houses but in lesser quantities than in occupied houses. This observation suggested that permanent broiler production would increase the danger of airborne diseases.

Although no figures or research data were submitted (*2*), the body weights and feed conversion were slightly better for broilers reared in pens sprayed with cottonseed oil at the rate of 5 gallons per 1,000 birds than in nonsprayed pens. The objective of oil spraying was to minimize the dust concentration because of dustborne respiratory diseases.

Data (*21*) obtained from four hatcheries (A, B, C, and D) indicated a positive correlation between general hatchery sanitation and livability of chicks from 0 to 2 weeks of age. The average sanitation score for hatcheries A, B, C, and D was, respectively, cleanest, intermediate, intermediate, and most contaminated with a corresponding mortality of 1, 3.3, 3.5, and 4 percent.

The presence of coli-aerogenes bacteria and molds in the fluff of chicks and poults in hatchers was very high, more so in that of poults than chicks, and in one case, this high degree of contamination was accompanied by a decrease in poult quality (*34*). Although fumigation of fluff and debris generally reduced the degree of contamination, not all organisms were destroyed because of the protection afforded by the dryness of the material.

Wildlife

A series of duststorms (*22*) caused death among waterfowl, quail, rabbits, pheasants, antelope, and one mule deer; the nostrils and windpipes of all dead animals were choked with mud. In another case, approximately 300 geese and 12 ducks alighted on the water of a shallow range pond a few inches deep in an effort to seek sanctuary from the duststorm, Rapidly filling with airborne silt, the pond became a mudhole; consequently the waterfowl colony perished.

During the height of one duststorm (*9*) strong-winged birds (geese, ducks) were able to fly away from the dust cloud, but the smaller, weaker birds were caught and perished. Large numbers of jackrabbits were found dead on the prairies during the next few days. No evidence of pathogenic organisms carried by the dust was found; the dust acted as an irritant to the mucous membranes of the respiratory tract. A statement that "crops and livestock losses have been large" should be clarified because no mention was made about livestock.

Inhalation of dust of two kinds (chemically active dust that is dissolved by tissue cells that then become poisoned and mechanically active dust that acts like a foreign body in tissues) was believed to be the cause of pulmonary diseases among zoo animals (avian and mammalian species). The pathological changes included anthracosis, silicosis, chronic bronchitis, fibrosis, lung gagrene, lung necrosis, and lung cancer (*1*, *47*). Besides asbestos dust inhalation, speculation on the causative agent of lung cancer in zoo animals included genetic susceptibility, long life span in capacity, improved nutrition, and improved diagnosis of disease (*47*).

Humans and Unspecified Animals

Numerous studies (*39*) have been carried out on the effect of cement dusts on humans, plants, and unspecified animals in France. Although respiratory diseases have been noted among cement workers, the studies indicated negative results among humans, plants, and animals living in the neighborhood of cement works.

EXPOSURE TO DUST INGESTION IN THE FIELD

Cattle, Sheep, and Dogs

Exposure of forage to cement dust in the vicinity of cement works has affected the health of cattle and the amount and quality of milk produced (*8*). The drop in milk yield occurred 1 or 2 days after the prevailing wind came from the cement works; this phenomenon was more pronounced when the herd lay northeast of the plant than when the herd lay southeast.

The cement kiln dust in the vicinity of another cement works (*36*) actually consisted of very finely ground limestone powder (29.3 percent limestone and 3.1 percent K_2O). When cows, sheep, and dogs were fed at levels of 2.5 to 11 g. per day of dust on the feed, no ill effects were observed during a 60-day period.

The detrimental effect of dust (fly ash) on cattle feed (*31*) was reflected in a 9.1 percent lower milk yield, an 8 percent lower milk fat, a 26.4 to 37.5 percent lower body-weight increase for 700 cattle in three localities. The number of abortions was 6.7 to 10 percent higher in polluted than in nonpolluted areas; hematological changes were also observed. The yearly dustfall in polluted and nonpolluted areas averaged 650 to 1,312 t./km.^{2} and 150 t./km.^{2}, respectively.

Swine

The post-mortem findings (*7*) of three pigs revealed: methemoglobinemia, hemorrhage in the gastrointestinal tract, pericardiac hemorrhage, acute universal stasis, cyanosis, nephrosis, lymphadenitis, and acute conjunctivitis. The source of poisoning was the presence of thick layers of dust in the ventilating shaft; this dust contained 0.38 to 1.1 percent nitrite, which came in contact with water that condensed on the shaft. The poisoned condensed water dripped to the floor where the pigs drank it.

Other Animals and Humans

The dust in cottonseed-oil mills contained 0.3 to 0.5 percent of gossypol that proved toxic to animals and humans when taken in large quantities with the food (*45*).

EXPOSURE TO DUST INHALATION OR INGESTION IN THE FIELD OR TO BOTH

A herd of Guernsey and Holstein cows on pasture near and on the windward side of a lime quarry and breaker exhibited extreme stiffness, shoulder defects, constipation, emaciation, tenderness in feet, and a 4.5- to 3.6-percent reduction in butterfat content of milk (*4*). Analyses made on pasture feed, corn silage, grain mixtures, and other feeds revealed no apparent deficiencies; some of the minerals (K, Mg, Fe, Mn, Cu) were somewhat high in the forage. The symptoms described are believed to be a result of a drift or dust from the lime quarry.

Exhaustive clinical, physiological, and pathological examinations (*43*) undertaken on 231 cattle in the dusty area of cement works revealed no significant effects of cement dust on the health and pregnancy of cattle.

EXPOSURE TO DUST INHALATION IN THE LABORATORY

Iron Ore Dust

Rats and dogs were exposed (*29*) to iron ore dust-contaminated air for 6 hours daily up to 16 months for rats and 24 months for dogs. A physiochemical analysis of the air showed that the dust contained 92.7 percent Fe_2O_3, 1.4 percent FeO, 5.5 percent SiO, 0.12 percent CaO, 0.03 percent MgO, 0.04 percent P_2O_5, and 16,000 to 18,000 dust particles per cubic meter of air. Results showed that (a) inhaled iron ore dust was phagocytized by "dust cells," which form "dust cell islands," (b) iron ore dust was eliminated via the bronchi and lymphatic channels, (c) accumulation of dust occurred in lymphatic vessels in different areas of the body, and (d) a disturbance in the oxidation reduction system, a reduction in the respiratory lung area, and an accumulation of products of tissue metabolism occurred along with a disturbance of dust-saturated lymph and blood circulation. The data suggested that iron ore dust per se possessed no toxic properties; it was the "lead" rock dust besides iron ore dust that was responsible for the pathological symptoms.

Aluminum (Al) Dust

Rats and rabbits were exposed (*26*) to an Al dust-contaminated atmosphere (5,000 dust particles/m.^{3}); rats also were given the Al dust via the trachea and rabbits via intravenous injection. The pathological changes observed as early as the 15th day after exposure included alteration of lung tissue and bronchial wall structures, interstitial fibrosis with hyalinosis in lung tissue, emphysema, hemorrhage, and pneumonia. These changes were highly specific and constituted a new type of pneumoconiosis—now designated as aluminosis. Al dust also caused fibrous degeneration of cardiac membranes, vessels, spleen, liver, and cerebral membranes.

Fiberglass-Plastic Dust

Continuous exposure (*41*) of guinea pigs, rats, and rabbits to fiberglass-plastic dust containing an average concentration of 338,000,000 particles (less than 10μ) per cubic foot of air for periods up to 25 months showed that: (a) dust was an inert material, (b) some tolerance was developed in most cases, (c) limited pulmonary reactions were restricted chiefly to guinea pigs, (d) the dust sporadically and moderately stimulated tuberculosis infection, and (e) no mortality resulted.

Uranium (U) Dusts

A 3-year inhalation program (*17*) with U dusts included more than 12,000 animals of six species: rats, mice, guinea pigs, rabbits, cats, and dogs. Two methods of exposure to the dusts—complete animal exposure and head exposure—were used. The animals were acclimatized to conditions in the exposure unit (conditioning period) for 6 hours per day, 6 days per week for 2 weeks if used in a 30-day study (acute) or for 4 weeks if used in a 12-month study (chronic). Dusts of 12 U compounds were tested at different concentrations (0.05 to 20 mg./m.^{3}). The results indicated that the greater the solubility, the greater was the toxicity of the U dust; the greater the concentration, the greater was the toxicity, irrespective of the solubility. The most characteristic of the complex pattern of response in U toxicity was the time lag between initial exposure and grossly manifest symptoms; this time lag depended on the solubility and concentration of the toxicant—usually within a week. Other symptoms included renal damages, occasional pulmonary damage, increase in nonprotein N and urea of blood, body-weight changes, and mortality. The order of susceptibility to U dust exposure for the six species of animals was: most susceptible, rabbit and cat;

intermediate, dog and mouse; least, guinea pig and rat. Because of possible ingestion of dust during inhalation exposure, studies were conducted to determine the ratio of the oral dose producing a toxicity equivalent to a given inhalation dose. On this basis, UO_2F_2 (highly soluble) and UF_4 (less soluble) were, respectively, 65 times and 10,000 times less toxic by ingestion than by inhalation. At inhalation exposure concentrations of 20 mg./m.^{3}, the enhancement of inhalation toxicity by ingested dust may be 15 percent with the more soluble dusts but not so with the more insoluble dusts.

EXPOSURE TO DUST INGESTION IN THE LABORATORY

Three groups of three cows each were fed 0, 0.3, and 1.8 kg. of fly ash per day in the fodder for a 3-year period. No ill effects were detected; in fact, fly ash tended to improve fertility (*35*).

EXPOSURE TO DUST INJECTION IN THE LABORATORY

Asbestos Dust

Attempts to puff asbestos dust into the air sacs of 2- to 6-year-old Leghorn fowl were not very successful (*37*); the fibers adhered to the moist surface of the air sac immediately, and, hence, the fibers did not penetrate far into the lung. However, if injected into the air sacs, the asbestos dust suspended in tributyrin reached the pulmonary alveoli; the immediate reaction was inflammation, probably because of the sharpness of the asbestos fibers. Tumors developed within a year after injection in several birds; many of the fibers remained unchanged after almost 4 years, and many were identified in the interalveolar septa of the lung.

Atmospheric Dust

The atmospheric dust was collected (*28*) from nine strategic locations, including the New York and New Jersey ends of the Holland tunnel. Subcutaneous injection into male C3H mice of 20 mg. of unextracted dust in saline did not produce sarcomas in 12 months. However, 50 mg. tar extracted from the atmospheric dust did produce sarcomas in the same period.

MISCELLANEOUS

Although not relevant to air pollution, the following information (*33*) should be of some interest from the physiological viewpoint. Extracts of cotton, flax, and hemp dusts and of the bracts of the cottonball did not release histamine from guinea pig, rat, cat, sheep, and pig lung tissue in vitro, but histamine was released significantly from human lung tissue in vitro under similar experimental conditions. Extracts of pericarps, another component of the cottonball, were without effect in both animal and human lung tissue; hence, the histamine-releasing activity of cotton dust is due to the presence of bract fragments in the cotton processed in the mills.

METHODS USED FOR DUST DETERMINATIONS OR EXPOSURES OR BOTH

The methods varied widely: filtration and sedimentation (*11, 46*), the formamide method (*20*), samplers (*2, 10, 16*), and exposures (*32, 38*).

RECOMMENDATIONS

The dust concentration in the atmosphere can be minimized by the use of scrubbers and filters in industrial plants, proper ventilatory and management practices within and without the farm buildings, and filters for automobile exhausts.

SUMMARY

Dusts appear to be of greatest concern to the health of poultry and zoo animals. Dust from duststorms, especially if moistened, can be fatal to wildlife. Toxicity of certain dusts was greater in the laboratory than in the field. The symptoms were restricted to the respiratory and gastrointestinal tracts. The smaller the particle size and the greater the density, solubility, humidity, activity of animals, and concentration of pathogenic airborne bacteria, the greater was the degree of toxicity. Prevailing winds, mineral content of dusts, and species of animals also influenced the degree of toxicity. With uranium dusts inhalation was much more toxic than ingestion of an equivalent inhalation dose, and the primary response to uranium toxicity was renal damage.

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Chapter 11.—Fluorides

Airborne fluorides (F) have caused more worldwide damage to domestic animals than any other air pollutant. The effects of the damages have been comprehensively reviewed (*4, 6, 25, 30, 44, 73, 75, 87, 116, 125, 135, 141, 160*). These reviews represent only a fraction of the voluminous literature on fluorides and their effects on domestic animals. Because of the voluminous literature, only a few representative references will be cited for each topic throughout the chapter. As indicated in the reviews, several terms had been used to describe the damages, namely fluorine intoxication, animal fluorosis, and industrial fluorosis. For the sake of clarity and brevity, the general term "fluorine intoxication," which covers all effects of fluorine in the animal system, will be used as the term to describe animal fluorosis and referred to hereafter as "fluorosis."

Sources of fluorosis included volcanoes (*48, 49, 135*); atmospheric contaminated feeds (*8, 30, 125*); mineral supplements high in F (*125*); emissions from the following industrial plants: phosphate fertilizer, aluminum, iron, or steel forges, and enamel frits (*44, 144*), tile (*27, 44*), brick kilns (*27, 144*), cryolite (*77*), and coal (*75*); and soil and water (*118, 125, 135*).

In the United States, fluorosis was found to be prevalent in four areas: Florida (*70, 91*), Tennessee (*3, 71, 95*), Utah (*56*), and Washington-Oregon (*105, 106, 154, 174*).

A majority of the cases of F poisoning in domestic animals was attributed to the ingestion of vegetation contaminated by F-containing industrial emissions rather than to inhalation of F-contaminated air (*5*). Prolonged exposure of vegetation before ingestion might result in an accumulation of toxic amounts of F from the atmosphere that itself is not particularly harmful by inhalation (*86, 114*) or that itself does not produce any apparent lesions on the foliage (*15*).

The degree of fluorosis in domestic animals as a result of ingestion of contaminated vegetation depends on numerous factors: direction of prevailing wind (*18, 23, 103, 159, 168*), distance of vegetation from the source of contamination (*15, 17, 75, 83, 98, 101, 109, 135*), amount of rainfall (*11, 103, 159*), age of animal (*6, 8, 71, 124, 150, 159, 176*), type and solubility of F (*150, 159*), concentration of F ingested (*124, 139, 150*), length of exposure (*124, 139, 150*), number of times of harvesting for hay (*159*), stress conditions (*139, 176*), individual biological response of animal (*139, 150*), presence of ions (*12, 176*), nutritional status (*139, 176*), the degree of refinement of cereal grains (*159*), enzymatic processes (*57, 88, 97*), and unknown factors (*176*).

The occurrence of F in air, food, water, animals, plants, and soils has been reviewed (*32*). Higher F values were noted in vegetation or tissues of domestic animals, or in both, in contaminated than in noncontaminated areas (*21, 37, 110, 113*). Nevertheless, a sound relation between atmospheric F contents and vegetative uptake is not evident because of the inadequate data on air analysis.[1]

A species difference was observed among domestic animals exposed to fluorosis. The rank of apparent decreasing susceptibility of farm animals was: cattle, sheep, horses, swine, rabbits, and poultry (*6, 120, 124, 125, 172, 173*). A discrepancy in the rank of susceptibility between dairy and beef cattle (*2, 28*) might be explained on the basis of measuring effects and degree of exposure. The fact that swine were unaffected on a farm where cattle, horses, sheep, poultry, and members of the farmer's family were affected casts a doubt on the reliability of the data (*114*). Horses, swine, and man are less affected than cattle to F toxicity, because food ingested does not remain in the digestive tract long enough to permit alimentary absorption of F as in cattle (*86*). Research indicated that the symptomatology was very similar between rabbits and cattle exposed to F (*73*). Since honey bees are kept on many farms, it is surprising that no information was available on the susceptibility of bees as compared with other domestic animals. The literature survey revealed much evidence of the very high susceptibility of bees to F-containing industrial emissions (see p. 45).

Fluorosis in domestic animals can be acute, or chronic. Acute F poisoning is rare among grazing farm animals, primarily because the animals voluntarily refuse to consume heavily contaminated forage that would have permitted an intake of acutely toxic amounts of F (*130*). However, in one study the acute symptoms of F poisoning included muscular tremors, unsteady gait, excitability, aggres-

[1] Personal communication from C. S. Brandt, research chemist, Crops Research Division, Agricultural Research Service, Department of Agriculture. 1969.

siveness followed by dermatitis, and sometimes conjunctivitis in cattle (*22*).

Typical clinical and pathological symptoms of F toxicity will be discussed for each class of domestic animals exposed to inhalation or ingestion or both of F in both the field and the laboratory.

EXPOSURE TO F INHALATION IN THE FIELD

The only specific information was a report (*1*) of a horse that was poisoned when the animal had accidentally remained 10 minutes in an outlet canal used for the condensation of hydrofluosilicic vapor. No details were given on the symptoms of the poisoned horse.

For cattle, the maximum permissible concentration of F inhalation in the field was 0.08 mg./m.^{3}; this value could also be used as a guideline for poisoning caused by ingestion of vegetation contaminated by industrial F (*142*).

EXPOSURE TO F INHALATION IN THE LABORATORY

Dogs

When dogs were exposed (*138*) to 6, 12.5, 25, 50, and 68 percent of the rat LC_{50} of 4,970, 2,690, 2,040, and 1,310 p.p.m. (4,065, 2,200, 1,673, and 1,072 mg./m.^{3}) for rats exposed to HF for 5, 15, 30, and 60 minutes, respectively, the toxicopathologic data revealed nonlethal effects, irritation of the tracheobronchia, conjunctiva, and nose, and no histological changes in the nonlethal ranges. One interesting observation was a persistent cough in dogs exposed to 25 percent of the LC_{50} value; the cough would reappear upon exercise after 2 days after exposure but would finally cease after 7 to 10 days.

Cats

In unpublished experiments, cats were found to tolerate without injury the inhalation of 0.1 mg./1. (100 mg./m.^{3}) of SiF_4 for 15 minutes (*45*).

Rabbits

Rabbits showed no harmful effects from chronic exposure (6 hours per day for 6 days) to 37 p.p.m. (30 mg./m.^{3}) HF; whereas, most people started to complain of the effects at 10 p.p.m. (8 mg./m.^{3}) (*86*). Exposure to 0.0245 mg./1. (25 mg./m.^{3}) HF for 41 hours caused no deaths despite internal damage: injury to cornea and nasal mucous membrane, dilation with congestion of heart, pulmonary hemorrhage and congestion, and edema and congestion of liver and kidney (*94*). A lower concentration of HF (0.0152 mg./1., or 15 mg./m.^{3}) for 309 exposure hours (that is, 6 or 7 hours per day, 5 days per week, for about 9 or 10 weeks) significantly lowered the erythrocyte counts, produced slight damage on lungs, liver, and kidneys, but had no apparent effect on the pregnancy and birth of normal progeny (*92*). Regardless of HF concentration and length of exposure, the F content was greatest in bone and teeth of rabbits; the F content sometimes reached as much as 10 times greater than normally expected at higher HF concentrations, which persisted as long as 15 months after exposure (*93*).

Exposure to esters of fluorophosphonates for 10 minutes at three concentrations (1/5000, 1/10,000, and 1/20,000) resulted in excessive salivation, nasal discharge, lacrimation, respiratory distress, convulsions, and death within ½ hour of the beginning of the 10-minute exposure (*81*).

Dogs and Rabbits

Dogs and rabbits were exposed to 0.5, 2, 5, and 16 p.p.m. (0.4, 1.6, 4.1, and 13.1 mg./m.^{3}) of elemental F gas for 35 days (*158*). At all levels the following symptoms occurred: irrational seizures in dogs; testicular changes and inflamed scrotal epithelium, coupled with subcutaneous hemorrhages around eyes and feet, in dogs; pulmonary damages in both rabbits and dogs; increases of F up to 200 to 300 percent in the jawbones of dogs. The higher three levels caused moderated to moderately severe pulmonary irritation in the rabbits and dogs. The highest level caused death of the rabbits and dogs.

EXPOSURE TO F INGESTION IN THE FIELD

Cattle

Symptoms

The symptoms of fluorosis in cattle have been well defined in the literature (*37, 116, 122*). In general, the acute symptoms included lameness, stiffness, lack of appetite and thirst, diarrhea, muscular weakness, and death. The chronic symptoms included dental changes, skeletal changes, lethargy, emaciation, poor health, and sometimes poor reproductive efficiency. Details on the symptomology follow:

Dental changes.—A preponderance of the literature has indicated dental changes among the first symptoms of chronic fluorosis in cattle. These changes occur as a result of ingestion of sublethal concentrations of F-contaminated forage for long periods. Chronic F ingestion interferes with the calcium (Ca) metabolism of the developing tooth, that is, before eruption; this interference results in incomplete formation of the enamel, the dentine, or the tooth itself. The normal translucency of the enamel is replaced in part or in total by a white chalky enamel, hence the term "dental mottling." Excessive F softens the teeth in such a way that dental wear develops, which interferes with mastication. Dental changes caused by F become permanent.

A positive relation between dental changes and the F content of teeth and bones of cattle has been established (*112*); however, the appearance of severely affected teeth should not be used as the sole criterion for F diagnosis.

Skeletal changes.—The absorption of F beyond the capacity of the body to handle the F results in calcification of the ligaments and in bony overgrowths, referred to as exostoses. These skeletal changes produce lameness, stiffness, and awkward gait—often with pain. Animals refuse to get up in advanced cases. An excess of 25 p.p.m. F in forage was needed to induce lameness in cattle (*14*). Skeletal changes due to F toxicity are many times indistinguishable from those due to other causes (traumatism, nutritional or hormonal deficiency, and others). Description of the skeletal changes has been well defined in the literature.

Body-weight changes.—Several studies (*104, 108, 141, 174, 180*) indicated that ingestion of F-contaminated vegetation for long periods resulted in a loss of body weight and finally in emaciation, but another study (*72*) did not show this.

Production and quality of milk and beef.—Many studies (*3, 4, 15, 18, 21, 27, 28, 37, 43, 44, 68, 70, 71, 77, 83, 104, 108, 115, 141, 143, 152, 169, 174*) showed that F reduced milk production, but one study (*76*) did not indicate any reduction. One possibility for the reduced milk yield was attributed to poor mastication as a result of excessive denture wear and to poor digestion of food as a result of F intoxication; consequently, F had no effect on the milk per se (*71*). The quality of milk was affected in terms of low butterfat (*68*). The market value of affected cattle was greatly depreciated, but the reasons were not clearly stated (*3, 21, 27, 43*).

Reproduction.—In several studies, ingestion of F-contaminated vegetation was observed to exert a detrimental effect on the overall reproductive efficiency (*3, 4, 21, 70, 83, 136, 174*). However, no adverse effects were observed in other studies (*17, 27, 72, 139*).

Other symptoms.—Loss of condition, lethargy, coarse hide, loss of appetite, cachexia, diarrhea, anemia, osteomalacia, and cessation of rumination have been associated with chronic fluorosis, as reported in the literature. Overgrown hooves were associated with F poisoning in one case (*174*) but not in another (*151*). One interesting uncommon symptom was that heavily affected cows lapped cold water like a dog rather than drank the water normally (*71*). In some cases bone lesions were not observed even though dental fluorosis was widespread in a herd of cattle (*17*). In other cases, chronic fluorosis decreased the hemoglobin level (*38, 66*) and esoinophile leukocytosis (*38*) and the Ca:P ratio of blood (*66*).

F content of normal and affected cattle

Teeth.—Fluorosis was suspected if the F content of teeth of cattle in a natural environment was 14 to 16 p.p.m. (*15*), two to 10 times more than that of controls (*49*), or if 50 percent of the incisor teeth were classified in grades 4 and 5 (*179*).

Skeleton.—The F content of bones of normal healthy cattle and their diseased counterparts was as follows: 45 and 259 to 781 mg. percent (*21*), 50 to 60 and 145 to 352 mg. percent (*113*), less than 600 and more than 3,000 p.p.m. (*141*), and 0.58 and 5.53

mg./g. dry weight (*104*), respectively. Fluorosis was suspected if cattle bones contained more than 4,000 p.p.m. of F (*179*) or two to 10 times more than that of normal animals (*49*).

Urinary values.—The urinary F content of healthy and affected cattle was: 2 to 6 and 16 to 68 p.p.m. (*15*), less than 5 and more than 10 p.p.m. (*141*), and 0.4 and 55.2 mg./1. (*21*), respectively. In one study, urine samples of catheterized and noncatheterized cattle exposed to F ingestion showed values of 23 and 89.6 mg.F/l., respectively, as compared with 0.354 to 0.361 mg./l. for controls (*84*). The urine of cattle eating forage containing 11 to 71 p.p.m. F showed a concentration of F up to 17 p.p.m. (*78*). The minimum F level in urine considered to be the critical point for fluorosis varied—10 p.p.m. (*15*), more than 10 p.p.m. (*18*), and more than 15 p.p.m. (*179*).

Tissues and milk.—No differences were observed in the F content of milk, blood, muscle, and liver of normal and diseased cattle (*49*). Muscle tissue and parenchymatic organs of affected bulls contained slight traces of F that would not threaten the consumer's health (*66*). The hide hair of cattle in high F-contaminated areas contained two to five times more F than that of cattle in low F-contaminated areas (*49*).

Progeny.—Metatarsal bones of calves born of normal cows showed an F content of 3.8 to 5.9 mg. percent as contrasted with 13 to 16.4 mg. percent for calves born of affected cows (*21*). The average F content of bones was 37, 30, 24, 32, 190, and 460 p.p.m. for 2- to 10-week-old fetuses, 4- to 9-month-old fetuses, day-old calf, veal calves, mature cows, and bone meal, respectively (*40*). The data suggest that small quantities of F are transferred to the fetus via the placenta of the cow and to calves through the cow's milk (*40*).

The F content of bones of newborn calves is dependent largely on the amount of F absorbed by the dam during the last 3 to 4 months of gestation and has no relation to the length of F exposure or the F content of her bones. A daily intake of 9 mg. F/kg. body weight/day by the dam does not produce a toxic effect in the calf via the placenta or milk (*137*).

Toxicity levels

A level of 5, 8, 14, and 98 p.p.m. F on pasture produced no dental changes, slight dental lesions in 25 percent of the cattle, dental fluorosis in 100 percent of the cattle, and bone and joint lesions within a month, respectively (*19*). The danger of F in hay fed to cattle may be regarded as harmful, suspect, and safe for excess of 50, excess of 25, and less than 10 p.p.m., respectively (*98*). Hay containing 0.01 to 0.1 percent F (100 to 1,000 p.p.m.) produced death in several weeks or months (*35*). Ingestion of up to 30 p.p.m. F in the daily forage was of no economic loss (*139*), 30 to 40 p.p.m. F was marginal (*139*), and an excess of 40 p.p.m. F produced damage and an economic loss (*139, 179*). The threshold of F toxicity for cattle is probably 2 to 3 mg./kg. body weight/day; the toxicity is greater on pasture contaminated with industrial F than in a feed concentrate containing F, with a grain supplement (*83*). The safe level for F in forage was no higher than 35 to 50 p.p.m. (*88*).

Sheep

Ingestion of F-contaminated vegetation has produced varying degrees of fluorosis in sheep (*4, 9, 15, 16, 17, 19, 22, 89, 108, 109, 153, 172*).

The clinical symptoms of sheep poisoned by F-ingestion were very similar to those of cattle: dental lesions, dental wear, exostoses, osteoporosis, ataxia, lameness, paresis, emaciation, diarrhea, and cachexia. Other symptoms not common with cattle but observed in poisoned sheep included conjunctivitis (*9*) and dermatitis with loss of wool (*22*).

The levels of F present on pasture required to produce fluorosis in sheep varied considerably: 16 p.p.m. produced dental fluorosis and abortion (*15*), 30 p.p.m. produced fluorosis (*2*), 44 p.p.m. within 1 mile from a factory induced dental and bone lesions in 62 percent of the sheep (*17*), and levels of 5, 8, and 14 p.p.m. caused no dental changes, slight dental changes in 25 percent of the sheep, and dental lesions in 100 percent of the sheep, respectively (*19*).

On three farms located ½, ¾, and 1¼ miles from an aluminum factory, 100, 62, and 46 percent of the sheep were affected, respectively (*16*). The lambs were not affected on the ½-mile farm; the forage of the ½- and ¾-mile farms contained 61 and 44 p.p.m. F, respectively. The F value for teeth and jawbone of affected sheep was 0.25 to 0.86 percent and 0.30 to 1.25 percent, respectively, as compared with 0.15 to 0.19 and 0.19 to 0.27 percent, respectively, for normal sheep. Ribs of affected sheep contained 18 p.p.m. F (*109*).

A lamb born of an F-poisoned ewe contained 3 to

11 and 33 times the F content of bones and teeth of an unexposed lamb, respectively. This high F content of the lamb is probably attributed to the placental transfer or to the ewe's milk, or to both (*89*).

Horses

Evidence of fluorosis among horses was documented in the literature (*2*, *11*, *22*, *49*, *70*, *71*, *76*, *77*, *90*, *172*). However, in two contaminated areas where cattle or sheep, or both, succumbed to F intoxication, horses showed no apparent damages of fluorosis (*15*, *77*); one possible reason for this may be that the horses on one farm did not graze as did the cattle but were fed the previous year's supply of dry fodder (*77*). On another farm where cattle and sheep were poisoned, two apparently healthy mares exhibited spontaneous fractures of the coxal bones (*22*). Lameness, pain, exostoses, emaciation, and bone fractures were symptoms associated with horses exposed to F ingestion (*76*, *172*). Symptoms of one horse exposed to F-contaminated water as a result of atmospheric F dust being washed down by the rain into the water receptacle included emaciation, dyspnea, extreme weakness, and excessive salivation; after death the pathological findings revealed hemorrhagic colitis, catarrhal enteritis, fatty degeneration of liver, severe lung emphysema, and a high F content of 1,500 p.p.m. in second phalanx and 1,060 p.p.m. in humerus bones (*11*).

The only F-poisoning symptom reported in horses grazing in contaminated areas was the higher citrate content of blood than in normal horses (*90*). Roughage containing at least 30 p.p.m. F on a dry basis produced fluorosis in horses (*2*). The F content was less in horses than in cattle when both species were kept in high F-contaminated areas (*49*).

Swine

In one area fluorosis was reported in swine as well as in horses and cattle; however, no symptoms were described for swine (*71*). In another area, pigs grazing on the same F-contaminated pasture as the cattle became afflicted with a stiff gait; the F content of the metatarsals was 92.6 and 41.9 to 44.5 mg. percent for the affected and healthy pigs, respectively (*21*).

Poultry

The only specific information on poultry exposed to F ingestion in the field was found in a report in which the F value of femurs from three specimens was 0.67, 0.27, and 0.40 percent (expressed in terms of ash as compared with 0.08 percent for a normal control (*15*). Broiler backs and necks from 19 processing plants averaged 15 p.p.m. F (8 to 21 p.p.m. range), which was about 20 times the F value in bone-free meat on a wet basis; the values for the corresponding feeds averaged 34 p.p.m., with a range from 17 to 56 p.p.m. (*133*).

Rabbits

An epidermal lesion occurred in rabbits fed forage grown in the industrial regions where livestock was affected with fluorosis (*101*).

Goats

HF poisoning among goats was observed (*76*) in the vicinity of a chemical plant manufacturing HF. The symptoms were lameness, pain, exostosis, lack of appetite, and emaciation. Prompt stabling of the animals brought relief and return to almost normalcy.

Honey Bees

Destruction of honey bees was associated with F-emitting industrial emissions (*4*, *23*, *29*, *42*, *61*, *62*, *76*, *101*, *103*, *113*, *168*). The symptoms more or less represented the acute type of F intoxication: muscular paralysis and high mortality over a period of time.

Poisoning of honey bees is more commonly associated with pesticides than with industrial emissions. Differentiation between the two sources of poisoning is important: pesticide poisoning results in a mass destruction of bees within a few days; whereas, atmospheric F intoxication slowly but steadily diminishes the bee population of affected apiary rows during the entire warm-weather season when F deposits accumulate on flowers and pollens. When F reached 10 to 214 mg. percent on plant surfaces and 0.9 to 2.8 mg. percent on pollens, the F values in dead bees varied from 2 to 33 mcg. per bee;

the lethal F concentration dose per bee was 4 to 5 mcg. (*103*). In another geographical area (*42*), a comparison of normal and poisoned bees revealed the presence of 7.39 and 23 to 47 mcg. F per bee, respectively. Where bee fluorosis occurred in the vicinity of an aluminum factory (*61*), apiaries relocated away from the factory lost fewer bees and became progressively less saturated with F, whereas those apiaries relocated closer to the factory lost more bees and showed an individual increase in F levels. Hence, the level of F per bee body is a function of the bee's activity and varies according to pollution level, geography, season, and activity and density of the flowering plants; the presence of more than 1 mcg. F per bee indicates the existence (permanent or intermittent) of a pollution source. Where bees had been poisoned near an aluminum factory in the LACQ area, no case of F poisoning in cattle had been verified (*23*).

Humans

In some cases when domestic animals exhibited fluorosis, human fluorosis was reported. The symptoms of which were one or more of the following: Dental mottling, respiratory distress, stiffness in knees or elbows, or both, a skin lesion, or high levels of F in teeth and urine (*11*, *36*, *53*, *101*, *114*, *152*). Man is much more sensitive than domestic animals to F intoxication (*135*).

EXPOSURE TO F INGESTION IN THE LABORATORY

Controlled feeding trials have been conducted with domestic animals to determine the minimum toxic levels of F required to produce different physiological and pathological symptoms of chronic fluorosis.

Cattle

Teeth and skeleton

A positive correlation was observed between dietary F and the F content in teeth (*140*) and in bones (*31*, *72*, *73*). The F content varied with the position of bone, with greater concentrations in the proximal than in the medial sections (*7*, *165*). The bone F also varied with the bone type, the cancellous type containing more F than the compact type (*167*). The F value in metatarsal ash was 0.10, 0.29, 0.57, and 1.04 percent for cattle fed 12, 27, 49, and 93 p.p.m. F as NaF on a dry basis, respectively; these data indicated a linear relation to the F level up to the 49 p.p.m. but a departure from linearity at the 93 p.p.m. level (*181*). The density values of bones were reduced by 22, 45, and 50 percent, respectively, on dietary F levels of 50, 70 and 100 p.p.m. as NaF; the calcium content of the bones followed the same pattern as the density values (*102*).

Dairy cattle fed a basal diet (3 to 5 p.p.m. F) for 5½ years stored less than 1,000 p.p.m. F in bone; in two groups fed 20 and 50 p.p.m. F as NaF, the increase in F content was 4½ and 10 times that of the basal group, respectively (*167*). Excess of 5,500 and 7,000 p.p.m. in compact and cancellous bone, respectively, was an indication of fluorosis. In fact, one of the most reliable measures of F toxicity was the presence of skeletal F levels in excess of 5,500 p.p.m. (*162*).

Body-weight changes

Two studies (*73*, *145*) indicated that body-weight gains were lowered if cattle were fed dietary F as NaF or other sources at levels in excess of 70 p.p.m., and another study (*72*) indicated that they were lowered at 200 p.p.m. The gains were not significantly affected if cattle were fed 12, 27, 49, and 93 p.p.m. F as NaF in 23 periods of 112 days each (*157*).

Milk production

Milk production was reduced in cows fed 49 or 93 p.p.m. of dietary F (*149*) and in other cows fed 75 to 250 p.p.m. of dietary F (*145*). Milk production was not reduced at a dietary level of 2.5 p.p.m. F of body weight (*140*) or when cows were given an abrupt feeding of 50 p.p.m. F (*122*). The milk yield was reduced by as much as 50 percent by the feeding of raw rock phosphate containing F (*128*).

Reproduction

Although a dietary level of 70 p.p.m. F or more reduced reproductive efficiency in one study (*73*), no adverse effects were observed in other studies (*128*, *149*). The progeny of treated cows were not apparently affected (*149*).

Quality of milk

The quality of milk was not greatly influenced by dietary F (*128, 149*). The F content of milk is always lower than that in blood and never exceeds 0.5 p.p.m. (*57*). When rock phosphate was fed to supply 0.022, 0.044, and 0.088 percent of F (220, 440, and 880 p.p.m.), the F content of contaminated milk (three F levels combined) was 0.11 to 0.26 p.p.m., as compared with 0.7 to 0.22 in normal milk; the contaminated milk exerted no detrimental effects on rat performance (*127*). Although the F concentration in milk increased with a corresponding increase in dietary F, the F values still remained within safe levels for consumption (*156*).

F content of tissues

When cattle (*31*) were fed raw rock phosphate to supply 0.022, 0.044, and 0.088 percent of F (220, 440, and 880 p.p.m.), the average F content of bone was 5,350, 6,400 and 9,500 p.p.m. of dry weight, respectively, as contrasted with 584 for controls. The thyroid glands contained 6.8, 890, and 1,640 p.p.m. of F on a dry basis for the three corresponding levels of F; the F content of liver, kidney, heart muscle, pancreas, tendon, hair, and hoof was less than 10 p.p.m. of dried tissue.

The F content of soft tissues of cows fed 0 and 50 p.p.m. F as NaF was 2 to 3 p.p.m. and approximately 4 to 9 p.p.m., respectively (*167*). Since soft tissues except the kidney do not retain increased quantities of F, time is required for a twofold to fourfold increase of F in soft tissues to produce toxic signs. Soft tissues become flooded with F after a saturation point of F has been reached in urine (70 to 80 p.p.m.) and in bones (15,000 to 20,000 p.p.m.). (The normal F levels are less than 5 to 10 p.p.m. for urine and 500 p.p.m. for bones.) When the soft tissues become saturated with F, the animal refuses to eat, which is a clinical evidence of F intoxication (*130*).

Physiological changes

Dietary F at a level of 3 p.p.m. of body weight reduced the hemoglobin and red-cell counts, hence producing anemia (*97*). No major changes were observed in the hematology of cattle fed 10, 25, 50, and 100 p.p.m. F as NaF (*74*) or those fed 12, 27, 49, and 93 p.p.m. F as NaF (*99*). However, on the 100 p.p.m. level, a slightly higher total eosinophil count and lower level of serum folic acid activity were observed (*74*).

At a F level of 2.5 p.p.m. of body weight, no toe enlargement, lapping of drinking water, or diarrhea were observed (*140*). No diarrhea occurred on a dietary level of 50 p.p.m. F (*121*).

The primary point of attack as a result of chronic fluorosis was the enzymatic systems of the body (*128*). Dietary F decreased the serum phosphatase (*97*) but increased the phosphatase activity in blood (*119*) and in bone (*107*).

Levels of dietary F up to 100 p.p.m. exerted no gross effect on hepatic function of dairy cattle for $5\frac{1}{2}$ years (*147*) and still no further effect on the gross, histological, or functional aspects of thyroids and liver of cattle for $7\frac{1}{2}$ years (*74*).

Dietary fluorosis disturbed the normal cellular respiration (*128, 129*) and increased the vitamin C concentration in the kidney, liver, anterior lobe of the hypophysis and the suprarenal cortex (*129*).

The F levels of 12, 27, 49, 93 p.p.m. in the diet for a $7\frac{1}{2}$-year period did not cause significant changes in the kidney glomerular filtration rates, but the three higher F levels did significantly reduce the p-aminohippuric acid clearance in the kidney (*99*).

The effects (*65*) of F ingestion on digestion and nutrient absorption are secondary on low levels of F (12, 27 p.p.m.) in long-term feeding trials ($7\frac{1}{2}$ years); $2\frac{1}{2}$ years are required for high levels of F (49, 93 p.p.m.) to influence digestion and nutrient absorption.

Time of intoxication

When cattle were fed 12, 27, 49, and 93 p.p.m. F as NaF on a dry basis for $7\frac{1}{2}$ years, the following observations were made (*149*): slight dental changes and slight periosteal hyperostosis were noted on the 27 p.p.m. level; moderate to marked dental lesions, slight to moderate osteofluorosis, bone lesions after $3\frac{1}{2}$ to 4 years and intermittent lameness after $4\frac{1}{2}$ years on the 49 p.p.m. level; and excessive dental and bone effects, bone lesions after $1\frac{1}{2}$ to 2 years, and intermittent lameness after $2\frac{1}{2}$ years on the 93 p.p.m. F level. The reduced milk yield on the 49 and 93p.p.m. levels always was preceded by clinical signs such as reduced feed intake, periosteal hyperostosis, and intermittent lameness.

Tolerance levels

The literature indicated discrepancies in the tolerance levels for cattle fed dietary F in the ration. A level of 50 p.p.m. F was tolerated in 4- to 6-year-old cows for as long as three lactations with no adverse effects other than mild exostoses and increased bone F content (*164*). Presence of 70 to 80 p.p.m. F in the urine was tolerated by cattle (*57*). Less than 49 p.p.m. F on a dry basis was tolerated by dairy cows for lactation in a 7½-year period (*65, 156*). Excess of 99 p.p.m. was tolerated for finishing beef cattle up to 2 years of age (56). Fluoride levels of 1.5 to 3 p.p.m. of body weight per day (as supplied by rock phosphate) were toxic (*39*), and levels of 3 to 6 g. F/day produced acute fluorosis with severe indigestion (*180*).

The critical F margin for overall performance of cattle appears to be 2 to 3 p.p.m. body weight (*120, 128*) or 30 to 50 p.p.m. F as NaF (*125*) and less than 1.6. p.p.m. of body weight per day for young dairy cattle (*162*). The tolerance recommendations for highly soluble F salts were 1 p.p.m. body weight and for poorly soluble F compounds, 60 to 100 p.p.m. F (*25*).

F and mineral interrelations

A low level of F (0.1 g. NaF/bull/day) (*96*) improved the retention of calcium (Ca) and phosphorus (P); whereas, a high level (1 g. NaF/bull/day) fed to bulls on a low P ration or a ration with a very wide Ca:P ratio (3:1 or 4.3:1) induced fluorosis. Addition of Ca or P salts in quantities to narrow the Ca:P ratio to optimum levels (2:1 or 1:1) protected the bulls for long periods against F intoxication. The feeding (*65*) of a high Ca-P mineral mixture at the rate of 3 percent did not lower the F retention in dairy cattle.

Diagnostic methods

Positive diagnosis of chronic fluorosis in cattle exposed to F ingestion can be made by several means: tail (14th coccygeal vertebra) biopsy, in which the animal does not have to be sacrificed (*34, 134, 161*); the quantity of plasma phosphatase (*119*); urinalysis (*72, 121, 140, 146, 149*); radiology (*132, 145*); the presence of F in feed, bone, and urine in relation to the five classifications of dental damages (*145*); calculation of the quantity of F ingested (*111*); and occurrence of clinical symptoms characteristic of F intoxication as described on the preceding pages of this chapter.

Since F ingestion carried a statistical weight of about 3 percent as a cause of the poor performance of cattle, husbandry practices, particularly breeding and management, were found to be twice as important as feed allowances as causes of the poor quality and performance of animals (*34*).

As preponderant data on fluorosis are being analyzed, an equation was developed (*148*) to determine the relation of combined independent variables (days, F in dry matter, F in dry fat-free rib, tooth classification) to their predicted expression of fluorosis in dairy cows, with correlation values being given for each dependent variable.

Since the diagnosis of chronic fluorosis is complex and dependent on many independent variables (p.41), evaluation of all effects of F toxicity would be much more effective than any single criterion (*56, 131, 157*).

Sheep

Young sheep fed an adequate diet of hay and oats supplemented with Naura rock phosphate furnishing 0, 60, 120, and 160 mg.F/day for 3 years exhibited the following effects (*117*): no deviations from normal health occurred on the 60 and 120 p.p.m. levels throughout the study, but some dental changes occurred on the 60 p.p.m. and dental lesions and exostoses occurred after 1 year on the 120 p.p.m.; on all F levels the incisors erupted at an earlier age, the amount of wool grown was not reduced, the bone ash content was not affected, and the F content in bones and teeth increased by 10 times; and the higher the F levels, the lower was feed consumption in many cases.

Growth was markedly depressed by a dietary F level of 6 p.p.m. of body weight per day and depressed to a lesser degree by smaller amounts of F (1.5 and 3 p.p.m. of body weight); the dietary F increased the iodine content in the thyroid glands (*67*). Levels of F as NaF up to 100 p.p.m. were not toxic in most cases; higher levels affected feed consumption and body weight gains in a 3-year period (*73*).

Rations with wide Ca:P ratios produced dental lesions similar to those observed in sheep affected with chronic fluorosis; differentiation between the two sources of dental lesions was made possible by the presence of F in teeth—the F content being 11 times greater in F-poisoned sheep than in sheep fed Ca-P imbalanced rations (*46*).

F retention was highly correlated with F intake; the F value in rib-bone ash was highly correlated with both F intake and F retention; the urine F output values (mg./day) were much more reliable than the urine F concentration (mcg./l.) (*69*).

The degree of chronic fluorosis in sheep was determined by the quantity of F in feed, bone, and urine in relation to the five classifications of dental damages (*145*).

The F tolerance limits for sheep are 70 to 100 p.p.m. (*125*) and 1.5 p.p.m. of body weight for the highly soluble F salts and 100 to 200 p.p.m. for the poorly soluble F compounds (*25*).

Poultry

Growth

Growth was not depressed, slightly depressed, and seriously depressed, respectively, in chicks fed F supplied by 1, 2, and 3 percent rock phosphate (*63*). Approximately 70 p.p.m. F on a body weight basis were necessary to inhibit growth of chicks after the first week of life (*123*). A decrease in body weight corresponded with an increase in the F level (0, 0.08, 0.10 percent F as NaF $\cong$ 0, 800, and 1,000 p.p.m.) fed to crossbred broiler male chicks in a 6-week period (*50*). Dietary F is not essential for normal growth in chicks but may be required for maintenance of enzyme activity at optimum rates (*178*).

Levels of 100, 200, and 400 to 800 p.p.m. F as NaF fed to 10- and 12-week-old turkey poults for a 16-week period produced no effects, decreased, and markedly decreased body weight gains, respectively (*8*).

Egg production and hatchability

The 3 percent rock phosphate level depressed egg production by approximately 8 percent; whereas, the 1 and 2 percent levels exerted no harmful effects; hatchability remained practically normal (*63*). The ingestion of 0.035, 0.07, and 0.105 percent F (350, 700, and 1,050 p.p.m.) supplied by rock phosphate did not affect egg size but did inhibit egg production (*126*).

Physiological changes

High F rations accelerated the coagulation time of blood in the chick (*80*) and thickened the intestinal tract wall of growing turkeys (*8*). The higher the F level, the greater were the size and weight of the proventriculus and the cellular changes in the gland surface (*50*). The serum F level plateaued after reaching 4 p.p.m. at the end of 1 week on a 900 p.p.m. F diet (*166*). Levels of 500 p.p.m. F as NaF or higher produced no significant changes in feed efficiency, total plasma protein levels, total plasma lipoproteins, percent fat utilization, or enzymatic activities (*178*).

F content of tissues

The F content of the following tissues of hens fed no dietary F, as measured in parts per million of dry tissue, was: kidney 6.5, liver 6.0, bone 612.5, muscle 4.6, and fat 0.9 (*64*). The femur ash F was 1,210, 10,800, 17,400, and 23,500 p.p.m., respectively, in 2-week-old chicks fed 0, 300, 600, and 900 p.p.m. F in a practical diet (*166*). The F content of egg yolk averaged 2.0, 3.0, and 3.1 p.p.m., respectively, from eggs laid by hens fed 0.035, 0.07, and 0.105 percent F (350, 700, and 1,050 p.p.m.) supplied by rock phosphate; the F content was much greater in the lipoid fraction than in the fat (*126*). The F concentration in eggshells depended on the F blood level during shell formation and could be as high as 51 p.p.m. (*57*). High levels of dietary F as NaF (400 to 800 p.p.m.) resulted in more than a twofold increase in F in the soft tissues of growing turkeys; the F content of bones increased with a corresponding increase in F level of ration and in length of time of feeding (*8*).

F and nutrition interrelation

The response to F in the diet is dependent on the composition of the diet (*166*). A comparison of a chick practical starter diet (25 p.p.m. F) and a purified diet (6 p.p.m. F) supplemented with 0, 300, 600, and 900 p.p.m. F as NaF showed that the serum F values were much lower for the purified diet than for the practical diet, irrespective of the dietary F level. A similar trend was observed for the femur ash values except at the 600 p.p.m. level, at which the F value was slightly higher on the purified than on the practical diet.

When day-old chicks were fed 0.08 or 0.11 percent F (800 or 1,100 p.p.m.) or magnesium (Mg) at the rate of 0.25, 0.50, or 0.90 percent (2,500, 5,000, or 9,000 p.p.m.) or both, the data (*51, 58*) indicated that the combination of F and Mg produced a greater growth depression than either one alone. Also, the chicks fed F and Mg developed a characteristic leg weakness and showed decreased calcification of bone, but these symptoms were not observed in chicks fed either F or Mg alone. The symptoms obtained with chicks fed the diets from hatch time on were not reproduced with chicks fed the same diets at 2 weeks of age. Later studies revealed that the F-Mg combination caused a greater reduction in the citric acid content of the bone than either one alone (*59*) and formed a stable complex that might inhibit an enzyme system involved in bone or muscle metabolism of the chick (*60*).

Tolerance limits

The F tolerance limits for poultry were 35 to 70 p.p.m. of body weight per day (*120*), 300 to 400 p.p.m. (*125*), and 100 and 250 p.p.m. of highly soluble F salts for broilers and layers, respectively, as contrasted with 300 to 400 p.p.m. of poorly soluble F compounds for chickens (*25*).

Swine

Symptoms

Levels of 30, 60, and 100 g. of NaF/100 pounds of diet for a 144-day period impaired growth and feed conversion; increased shaft diameter, caused loss of color and luster, induced exostoses, and decreased breaking strength of the femurs; enlarged mandibles—which were attributed to an increased bone marrow cavity rather than a thickened bone wall; and softened the teeth (*79*). Similar results were observed with swine fed levels more than 0.029 percent F (290 p.p.m.) as NaF or 0.033 percent F (330 p.p.m.) as rock phosphate, except that the mandibles were not enlarged; other symptoms included poor lactation, diuresis, and degeneration of epithelium of kidney tubules (*80*). Dental lesions, high F content in bone and teeth, and macroscopic changes in kidneys were observed in pigs fed 15 p.p.m. of F, on a body weight basis, per day for 168 days (*135*).

High levels of dietary F (1,000 p.p.m.) reduced the appetite and interfered with calcium metabolism and bone growth of 120- to 150-day-old pigs (*33*) and produced rachitomimetic-like effects on the skeletal tissues of growing pigs (*13*).

Studies with growing pigs fed 26 p.p.m. of F in dry feed showed that the relative values of F retention and excretion were not related to body weight, although the absolute values increased with the weight of the animals (*82*).

Tolerance limits

The F tolerance levels for swine were 8 to 10 p.p.m. of body weight/day (*120*), 70 to 100 p.p.m. F (*125*), and 70 p.p.m. of highly soluble F salts or 100 to 200 p.p.m. of poorly soluble F compounds (*25*).

Rabbits

Retarded growth, stiffness, and dental changes characteristic of fluorosis became apparent in 4 months when rabbits were fed rations containing more than 0.021 percent F (210 p.p.m.); such physiological processes were not affected if the F retention in the body did not exceed 5,000 p.p.m. (*24*).

Dietary F increased the F content of teeth and bones by five to eight times and of hair, blood, heart, spleen, brain, and muscles by two times as high as that of those in control rabbits; no differences were noted in the F content of liver, kidney, and lungs (*49*).

Data with rabbits fed 0, 50, 100, 200, and 300 p.p.m. F as NaF in a diet containing 46 p.p.m. F revealed that the placenta was an extremely efficient barrier to the passage of F and that the alkaline phosphatase activity in plasma, kidney, liver, bone, and intestinal mucosa was not a suitable criterion of the degree of fluorosis (*100*).

Ingestion of 5 or 50 p.p.m. F on a body weight basis resulted in a most intense osteoplastic action (periosteal neoformation, spongy compacta, fibrous bone with coarsely grained calcification, decreased elasticity, reduced bending strength), attributable exclusively to the F-cation, regardless of the F compound involved; the F compound involved the joint action of alimentary factors and extra-osseous organic damage that would lead to severe generalized disease and death (*175*). Fluoride from rock phosphate was as toxic as an equivalent level of F from NaF if not more toxic (*24*).

Chronic F poisoning (25 p.p.m. F on a body weight basis per day for 12 days, then none for 15 days, and finally 10 p.p.m. for 57 days) produced a rise in the blood cholesterol level, an intensified experimental hypercholesteremia, a reduction in body weight and blood Ca levels, anemia, and an increase in reticulocytosis; hence, there is a possible relation between fluorosis and atherosclerosis (*85*).

Dogs

One dog fed 80 p.p.m. F on a body weight basis per day for 587 days and another one, 14 p.p.m. F for 626 days exhibited osteomalacia, a high F content in teeth and bones, macroscopic changes in kidneys, and severe anemia (*135*). The younger the age, the greater the daily dose (0 to 0.4 g./dog/day), and the greater the length of time of F ingestion (46 to 128 days), the greater was the effect on dental and bone changes; puppies exclusively fed the milk of their chronically F-poisoned mother dogs for 28 days exhibited dental and bone changes typical of rickets; hence, roentgenographic examination of skeletons was recommended to distinguish fluorosis from nutritional rickets (*10*).

Studies (*54*) with 21 litters of dogs showed no significant alteration in serum Ca and P, hemoglobin, blood-coagulation time, and growth when the dogs were fed for as long as 1 year 5 p.p.m. F on a body weight basis per day as supplied by NaF, purified bonemeal powder, and defluorinated phosphate. Dental fluorosis and F retention in bones were much greater with NaF than with the other two F sources. However, both bonemeal and defluorinated phosphate produced stronger teeth than did the control diet containing an equivalent quantity of Ca and P as found in bonemeal or defluorinated phosphate.

Species Differences

Radioactive F administration (*57*) produced a peak in the maximum blood level of F by the second hour for sheep as compared with the fifth hour for cattle; the peak represented 1 percent of the amount administered. The prothrombin time was not affected in cattle fed a single dose of 30 mg. F from NaF/kg. body weight or fed continuously a dose of 3 mg. F from NaF/kg. body weight. In chickens the prothrombin time was reduced from 20 to 16 seconds and the blood-coagulation time from 96 to 73 seconds when 350 p.p.m. F was fed.

Fluoride retention in the hen is much less than in dairy cattle, as supported by the data that dietary F at the rate of 0.088 percent (880 p.p.m.) fed to cattle increased 16 to 25 times the F content of bone, as contrasted with 13 to 14 times that in bones of chickens fed 0.0156 percent F (156 p.p.m.) (*64*).

The large increase in serum F in the chick fed 300, 600, and 900 p.p.m. F is in sharp contrast to the efficient homeostatic F control noted in most species, none of which were identified (*166*).

Comparison of Sources of F

When both salts were fed at comparable F levels, F as NaF was more toxic than F as CaF_2 for cattle (*107*) and for poultry and swine (*80*). Rock phosphate, phosphatic limestone, and treble superphosphate were intermediate between NaF and CaF_2 for poultry and swine (*80*). F as NaF was more toxic than an equivalent amount of F supplied by rock phosphate, hay or pasture for cattle (*72*) and just as toxic as F on contaminated vegetation, if not more toxic (*73, 150*). Florida rock phosphate supplying 170 mg. F/day was less toxic in all respects than Naura rock phosphate supplying 160 mg. F/day for sheep (*117*).

More F was deposited in bones of cattle fed 67 p.p.m. F as NaF than in bones of cattle fed 134 p.p.m. F as CaF_2; however, greater F deposition in bones occurred on 134 p.p.m. F as soft phosphate than on 67 p.p.m. F as NaF (*7*). The mean F retention in sheep was 36.7 and 38.6 percent of the daily intake of dicalcium phosphate and mineral phosphate, respectively (*69*).

Comparison of Results Obtained in the Field and the Laboratory

Cattle

The performance of beef cattle fed up to 38 p.p.m. F as NaF in drylot was just as satisfactory as that of those on pasture containing 44 p.p.m. F and fed hay containing up to 66 p.p.m. F (*72, 73*). Diarrhea was observed in cattle on pasture and in cattle in controlled feeding trials in drylot in which 64 p.p.m. F on a body weight basis was fed (*37*). No detrimental effects of chronic fluorosis on reproduction and parturition were shown in controlled studies conducted in the field and the controlled studies conducted in the field and the laboratory (*139*).

The excellent correlation of results obtained with cattle both in the field and the laboratory would suggest the possibility of delineating herds or areas in which damaging or nondamaging effects of F might be expected (*179*). However, symptoms and lesions diagnostically significant for fluorosis in suspected areas were also observed with approximately the same frequency in nonsuspected areas

(*28*, *139*). Thus, the complexity of the fluorosis picture becomes apparent.

Swine

Studies with swine fed 0.014, 0.0217, 0.293, and 0.0569 percent F (140, 217, 293, and 569 p.p.m. supplied by rock phosphate) both on pasture and in drylot showed the following results (*41*): the rate of gain was affected by the highest F level only on pasture and by the three higher F levels in drylot, and feed efficiency was decreased by the highest F level both on pasture and in drylot.

EXPOSURE TO F INJECTION IN THE LABORATORY

Dogs

Intraveous injections of single doses of 5 to 20 p.p.m. of NaF on a body weight basis produced diuresis and alkalinity of urine in dogs; no microscopic evidence of renal damage was present (*52*). Dyspnea and lowering of blood pressure from 170 to 136 mm. Hg. were produced by intravenous injections of 1.5 to 5.3 p.p.m. F as NaF on a body weight basis and of 16 to 31.7 p.p.m. F on a body weight basis, respectively (*55*).

Chickens

The tolerance to intraperitoneal injections of F (35 to 40 p.p.m. F on a body weight basis) was lower than ingested levels (70 p.p.m. F on a body weight basis) for growth retardation in chicks; an injection of 64 p.p.m. F on a body weight basis was lethal (*123*).

The injection method of 0.5 mg. NaF/day resulted in one-half as much as F storage as did the stomach tube method (2 mg. NaF/day); this observation indicates a lower metabolic availability of F by the oral route (*14*).

MISCELLANEOUS

A literature review was presented to indicate that F was one of the industrial poisons that lowered the immunobilogical response of man, pigeons, rabbits, and other animals against certain diseases, such as typhoid fever, anthrax, tuberculosis, and *Staphylococcus aureus* (*47*).

ALLEVIATORS

The role of F alleviators in reducing the effects of chronic fluorosis in farm animals has been reviewed (*19*, *177*). Most of the effective alleviators are of nutritional origin, and others pertain to management practices. Probably the most widely used nutritional alleviator for treatment of chronic fluorosis is aluminum (Al) salts, primarily the sulfate or chloride salt (*12*, *19*, *20*, *56*, *72*, *88*, *96*, *124*, *125*, *169*, *170*, *171*, *177*). In some cases, the F retention in bones was reduced by as much as 30 to 45 percent (*56*, *171*). The aluminum salts are provided to cattle in the form of cakes.

Calcium or phosphorus compounds, or both, are also effective as F alleviators (*2*, *57*, *77*, *96*, *124*, *125*, *177*). Although many Ca compounds are effective, they are not so effective as Al compounds (*19*); in one study, calcium aluminate actually increased the mean F content of bones of affected cattle over that of normal cattle (*20*). The addition of 50 g. of calcium per day per cow in a volcanic area slightly reduced the F content in the hair and blood in a 10-month period (*48*).

High planes of nutrition such as protein, vitamin C, and minerals (*27*, *124*, *125*, *163*, *177*), the use of clean, uncontaminated green forage or roughage very low in F, or both, (*2*, *27*, *41*, *43*, *77*, *124*, *125*, *163*, *170*, *177*), and liberal grain feeding (*124*) are other effective alleviators. The use of iodized salt as a block was ineffective (*67*).

Management practices involved crop rotation (*2*), a switch from cattle and sheep to swine and poultry in heavily contaminated areas (*27*, *172*), the maintaining of mature cattle only on contaminated pasture (*169*), and confinement of animals in barns (*76*). Breeding of F-susceptible strains of cattle, sheep, and bees was discouraged (*62*).

Injection of atropine (10 mg./kg.) was effective in rabbits if given 10 minutes before inhalation of fluorophosphonate but not if given after inhalation (*81*).

Regardless of the type of alleviation, complete prevention of the toxic effects of F ingestion by farm animals is an impossibility. However, the effective alleviators can counteract fluorosis to such an extent that the farm animal can be rendered serviceable to the farmer from an economic standpoint.

CONTROLS OF ATMOSPHERIC F EMISSIONS

Special equipment (scrubbers, waste-gas purifiers, and others) have been installed by different industries to reduce to a minimum the quantity of F being emitted into the atmosphere. Such installation was effective in most cases (*26, 76, 91*) but not effective in another case (*113*). One industrial plant was able to reduce the F emission below that allowed by the air pollution law in Florida (*91*); another industry was able to keep the F emissions within a 100 to 2,000-meter area of the plant and in the direction of the prevailing wind only (*76*).

Analysis of air, vegetation, and tissue of farm animals should be taken in areas where a new factory is to be located before the operation of the factory to establish the local prevalence of fluorosis and other diseases that might be confused with fluorosis (*155*). Such data would prove invaluable to owners of farm animals, especially in lawsuits, should the animals become poisoned later on by atmospheric F pollution.

Air-quality standards based on atmospheric F levels are not feasible as a means of protecting farm animals from F toxicity; however, guidelines based on the atmospheric F levels or urinary F content might serve to protect farm animals in a community and be acceptable to F-emitting industries (*159*).

SUMMARY

Fluorosis occurs worldwide, with four well-defined areas in the United States, namely, Florida, Tennessee, Utah, and Washington-Oregon. Sources of fluorides that cause fluorosis are industrial emissions, volcanic gases, and presence of F in soil, water, minerals, and feeds. Intoxication of farm animals may result from inhalation or ingestion, or both, of atmospheric F; however, a preponderance of the literature suggests that the primary cause of F toxicosis is a result of ingestion of F-contaminated vegetation. The degree of F intoxication was found to depend largely on the quantity of F deposited on vegetation, which is influenced by meteorological conditions (prevailing winds, rainfall, topography), activity of industry, and time elapse between harvesting. Besides the quantity of F ingested other agents that influence the degree of fluorosis were age of animal, length of time of exposure, type of solubility of F, presence of ions, nutritional status, stress, health status, F content in feed concentrates being supplied to animals on contaminated pasture, and unknown factors. Intoxication of F was apparently associated with interference of calcium metabolism and normal cellular respiration, inhibition of certain enzymatic processes, and reduction of the immunobiological response of the animal to certain diseases.

The rank of decreasing susceptibility to fluorosis in farm animals was cattle, sheep, horses, swine, rabbits, and poultry. The literature suggest that honey bees might be more susceptible than cattle. No information was available on the susceptibility of dogs and cats in relation to the other farm animals. Although a discrepancy appears in the literature about the F tolerance limits, the following limits should give an indication of the tolerance requirements (p.p.m.) via ingestion of farm animals: 30 to 50 for cattle, 70 to 100 for sheep, 70 to 100 for swine, 150 to 300 for broilers, and 300 to 400 for hens. The tolerance limits were lower for highly soluble than poorly soluble F compounds. The presence of more than 1 mcg. F per bee indicates danger of pollution.

Symptoms associated with F inhalation or ingestion, or both, have been well defined in the literature. In general, the acute symptoms included lameness, stiffness, lack of appetite and thirst, diarrhea, and muscular weakness, the chronic symptoms involved

dental lesions, skeletal changes lethargy, emaciation, poor health, and sometimes poor reproductive efficiency; death often occurred.

Experimental studies with dietary F confirmed many of the symptoms found in the field. However, several discrepancies occurred with respect to certain symptoms. The differences observed in the field and the laboratory could be attributed to the difference in number and type of independent and dependent variables involved. One of the variables that might account for the discrepancy in the F content of tissues (e.g., a lethal concentration of 4 mcg. F per bee as contrasted with a normal concentration of 7 mcg. per bee) is the measuring effect. Although dietary F did increase the F content in teeth, bones, soft tissues, and milk, the content usually fell within the safe limits for human consumption.

Comparison of identical feeding trials with F in both the field (pasture) and the laboratory (drylot) suggested less damage in bovine dental lesions and better growth in swine on pasture than in drylot.

Differences between domestic animals were noted: (a) the F being ingested by the pregnant cow or ewe was transferred to the offspring via the placenta or via the mother's milk; this was not observed with rabbits; (b) a peak in the maximum blood level of F occurred by the second hour for sheep and by the fifth hour for cattle; the peak represented 1 percent of the amount administered; (c) the prothrombin time was affected in chickens but not in cattle; (d) the F retention was less in the chicken than in the cow; (e) the large increase in serum F in the growing chicken was in contrast to the efficient homeostatic F control in most species of animals.

The diagnosis of chronic fluorosis is very complex and depends on many variables. The criteria for F poisoning include tail vertebrae biopsy, urinalysis, radiology, roentgenography to differentiate fluorosis from rickets, traumatism and other leg deformities, plasma phosphatase index, presence of F in feed, bone, and urine in relation to dental lesion scores, quantity of F ingested, and the macrosymptoms observed on pasture (lameness, stiffness, etc). The veterinarian should analyze all these criteria rather than rely on any one criterion in diagnosing the disease. Even so, symptoms and lesions diagnostically significant for fluorosis in suspected areas were also observed with approximately the same frequency in nonsuspected areas.

Aluminum salts have proved very effective in keeping the effects of chronic fluorosis under control so that the economic value of domestic animals would not be greatly reduced. So are many calcium salts. Other recommendations to protect domestic animals from further damage include high planes of nutrition, feed supplements low in F, uncontaminated green forage, close confinement of animals, crop rotation, switch from cattle and sheep to swine and poultry in heavily contaminated areas, use of mature animals only on contaminated pasture, and discouragement from breeding of highly susceptible individuals in cattle, sheep, and bees. These alleviators, no matter how effective they may be, do not completely prevent chronic fluorosis in domestic animals. Industrial cooperation is essential in minimizing the quantity of atmospheric F emissions through the use of scrubbers, waste-gas purifiers, or other mechanical equipment.

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Chapter 12.—Hydrocarbons (Organics)

Hydrocarbons (HC), composed of carbon and hydrogen in different proportions, have many uses in industry. Petroleum and natural gas are two natural sources of HC; when further refined, petroleum yields gasoline and kerosene, both of which are used for fuel. The incomplete combustion of such fuels produce large quantities of components—CO, NO, NO_2, SO_2, other HC, and others—being discharged into the atmosphere. The literature survey revealed very little information on the biological effects of HC on domestic animals in the field. Nevertheless, considerable research had been conducted with laboratory animals, including the dog and rabbit. Some of these results will be discussed briefly. The interdependence of HC with other air pollutants is discussed in other chapters.

EXPOSURE TO HC INHALATION OR INGESTION IN THE FIELD OR TO BOTH

In 1 week in March 1968, over 6,000 deaths occurred among sheep grazing in the Skull Valley; none were affected outside of the Skull Valley grazing area (*1*). Later investigations revealed dead rabbits, rodents, and birds near the affected grazing area. Analysis of sheep carcasses and forage revealed the presence of a nerve gas agent (Sarin) used by the Army Dugway Proving Ground approximately 30 miles west of the grazing site. Such nerve gas agents kill animals by blocking the action of cholinesterase, which is needed to suppress another chemical that causes muscular convulsions. Veterinarians who worked with the dying sheep developed symptoms similar to those of the flu as well as that of nerve gas toxicity (nausea, headaches, dizziness, diarrhea). A large number of patients had been treated for an overdose of anti-cholinesterase agents in a hospital 50 miles east of the Army proving ground. Settlement has been made to a firm in Utah for the nerve gas damage to the sheep (*8*).

EXPOSURE TO HC INHALATION IN THE LABORATORY

Benzene or Its Derivatives

Inhalation of benzene or its derivatives produced the following symptoms: carcinogenic lesions in mice exposed for 1 year to 1.4 mg./m.^{3} of 3, 4-benzpyrene from tar fumes (*10*); decreased phagocytic activity, reduced erythrocytes, increased leucocytes, and reduced body-weight gains in rabbits exposed 3 hours daily for 3 months to benzene vapor at a concentration of 0.02, 0.05, 0.2, and 0.5 mg./l. (20, 50, 200, and 500 mg./m.^{3}), sluggishness at all concentrations except the lowest, and hemorrhage of lungs, stomach, and kidneys, flabby livers, and pale bone marrow of tibia at the 200 and 500 mg./m.^{3} concentrations (*20*); enzymatic changes, reduced erythrocytes, increased leucocytes, disturbed antagonistic muscle chronaxy ratios, and a lowered coproporphyrin elimination in urine in rats exposed continuously for 70 days to 0.05 and 50 mg./m.^{3} of styrol, a benzene homologue (*18*); enzymatic changes, reduced erythrocytes, and increased leucocytes in rats inhaling benzol for 130 days at a concentration of 0.1 mg./l. (100 mg./m.^{3}), for 28 days at 1 mg./l. (1,000 mg./m.^{3}), and for 7 days at 2.5 mg./l. (2,500 mg./m.^{3}) (*5*).

2-Chlorobutadiene-1, 3

Exposure of rabbits for 4 hours daily for a 4-month period to 2-chlorobutadiene-1, 3 beginning at the rate of 0.1 mg./l. (100 mg./m.^{3}) and gradually increased to 0.5 or 0.6 mg./l. (500 or 600 mg./m.^{3}) reduced the liver glycogen content (*12*). Dogs given similar treatments, beginning with 0.5 mg./l. and gradually decreased to 0.1 mg./l., exhibited a rise in the blood pyruvic acid level, which indicated disturbed carbohydrate metabolism. This disturbance was partially counteracted by 1 mg. of thiamin per day.

Dimethylformamide

Exposure of rats continuously for 2 months to 0.5 and 10 mg./m.^{3} of dimethylformamide brought about significant reduction in the cholinesterase activity and a drop in the rate of coproporphyrin elimination in the urine; growth, behavior, and health were not affected (*13*).

Dioxan

Severe toxic effects of 1:4 dioxan were observed (*4*) in guinea pigs, rats, mice, and rabbits exposed at the concentration of a 1/100, 1/200, 1/500, and 1/1,000 mixture of dioxan/air for ½, 1, or 2 hours daily 5 days per week. The outstanding observations were severe lesions in kidneys and liver at all levels, damage to the respiratory tract only at the very high concentrations, and death within 3 hours after exposure at the 1/100 level.

Formaldehyde and Its Homologues

One-hour exposures of guinea pigs to 0.3 to 50 p.p.m. (0.37 to 61 mg./m.^{3}) of formaldehyde or to 0.3 to 50 p.p.m. (0.56 to 94 mg./m.^{3}) of formic acid produced an increase in resistance and a decrease in compliance, statistically significant at concentrations as low as 0.3 p.p.m. Formic acid was more potent than formaldehyde as a respiratory irritant (*2*). Formaldehyde was detected in the atmosphere at a concentration of up to 0.042 mg./m.^{3} at 1,000 meters from the formalin manufacturing plants and of 2 to 10 mg./m.^{3} (mean of 2.6) on sidewalks 1 to 2 meters from a running vehicle motor; the maximum permissible single formaldehyde concentration in the air should not exceed 0.035 mg./m.^{3} (*9*).

Gasoline

Male white rats were exposed to 0, 20, and 100 mg./m.^{3} concentrations of gasoline vapor 6 hours daily for over a period of 5 months (*7*). The highest concentration elicited changes in the conditioned reflex activity, the intensity of which increased with the duration of the exposures and which disappeared only 2 weeks after discontinuation of exposure. Later studies (*7*) with humans indicated that the threshold of olfactory gasoline odor perception was the most sensitive index for the determination of limits of allowable concentrations of gasoline vapor in the air—5 mg./m.^{3} calculated as hydrocarbons.

Monkeys, dogs, rabbits, and guinea pigs were exposed to inhalation of 0.3 percent of straight gasoline and of ethyl gasoline vapors for 2 hours (*16*). The clinical symptoms were unsteadiness, drowsiness, lacrimation, nasal discharge, and sometimes depression; the pathological examinations revealed hyperemia of lungs and liver, kidney degeneration, pancreatic congestion, and splenic anemia. Moderate dizziness was observed in service station employees exposed to gasoline vapors at the rate of 0.3 percent in 30 minutes.

Ketenes

In one series of experiments (*19*), the highest level that could be inhaled without inducing a fatal degree and the least concentration that induced death, respectively, for the following species in p.p.m. (mg./m.^{3}) were: mouse 25 (43) and 50 (86), monkey 50 (86) and 200 (344), rat 250 (429) and 375 (644), guinea pig 375 (644) and 500 (859), cat 200 (344) and 750 (1,288), and rabbit 750 (1,288) and 1,000 (1,718). The gross and microscopic lesions (alveolar edema and congestion, emphysema, hemorrhage, pneumonia) could be correlated with signs of intoxication and death.

Methane

Dogs, monkeys, and guinea pigs were exposed to air containing 20 percent by volume of dichlorodifluoromethane vapor (130,879 mg./m.^{3}) for 7 to 8 hours daily 5 days per week and 4 hours on the sixth day of each week during a 12-week period (*17*). Mild to moderate to marked generalized tremor occurred in dogs, and mild to moderate generalized tremor occurred in monkeys. Both species behaved like drunkards while walking. Slight changes in body weights and number of red blood cells and hemoglobin of dogs and monkeys occurred the first 2 or 3 weeks of exposure, after which the body weights and hematological values returned to normal. Guinea pigs exhibited none of the significant symptoms; in fact, normal reproductive efficiency was observed in exposed as well as in control guinea pigs.

Nitro-Olefins, Conjugated

Rabbits, rats, and chicks were exposed for a 5-hour period to 11 different nitro-olefins (*3*). The concentrations varied with the nitro-olefins tested: one concentration was used for one nitro-olefin and two, three, or four concentrations for the other nitro-olefins. Most of these concentrations were not uniform for all nitro-olefins; the lowest and highest concentration were 0.10 and 5.8 mg./l. (100 and 5,800 mg./m.^{3}). The data indicated that all the nitro-olefins tested at the higher concentrations were very toxic: marked irritation of entire respiratory tract, skin, eyes; hyperexcitability; tremors; clonic convulsions; tachycardia; increased rate and magnitude of respiration followed by depression, ataxia, cyanosis, dyspnea; and death. The pathological changes were most pronounced in lungs. Of all nitro-olefins tested, those with short C-chains were more toxic.

Phosgene

Phosgene via inhalation is toxic to man and dogs at or above 0.10 to 0.45 mg./l. (100 to 450 mg./m.^{3}); it acts as an irritant, which causes tears and coughing, as well as a suffocant, which causes pulmonary edema (*21*).

EXPOSURE TO HC INJECTION

Equally toxic effects were obtained with 1:4 dioxan, irrespective of the method of administration—inhalation, intravenous injection, or ingestion (*4*).

Intratracheal injection of 25 ml. of methylcholanthrene suspended in a 1 percent aqueous solution of polysorbate 80 induced pulmonary neoplasma in ducks (*14*). The concentrations of methylcholanthrene were 62.5, 125, and 250 mg. per 25 ml. injection. The first tumor appeared 56 days after injection.

When cats and rats were subcutaneously injected with 100 p.p.m. of orthonitrochlorobenzene, the following effects were noted (*6*): methemoglobinemia, acidosis, altered dehydrogenase activity, hypothermia, and death. These effects were largely counteracted by injection of ascorbic acid mixed with sodium nicotinate (5 p.p.m.) and riboflavin (0.4 p.p.m.) 30 minutes after the orthonitrochlorobenzene injection. Intravenous injection of vitamins was more effective than subcutaneous injection.

Benzene and its amino- and nitro-derivatives depressed immunobiological reactions from typhoid fever vaccination in rabbits in acute and chronic stages of intoxication as a result of subcutaneous injection of the HC. The benzene derivatives proved more active than benzene (*11*).

EXPOSURE TO HC INGESTION IN THE LABORATORY

Levels of 0.1 to 2.5 mg. benzpyrene per gram of feed (100 to 2,500 p.p.m.) had no effect on growth, livability, feed consumption, and egg production of chickens (*15*). However, the skin, feathers, viscera, and eggs exhibited a blue fluorescence, which disappeared within 6 days after benzpyrene withdrawal. The blue fluorescence may be due to either benzpyrene or one of its metabolites being absorbed from the intestine and metabolized within the body. (Note: This publication (*15*) stated that the chickens are being observed for effect of the HC on development of neoplasm.)

SUMMARY

The literature survey indicated a paucity of information on the biological effects of hydrocarbons on domestic animals in the field. Inhalation studies with laboratory animals revealed a variation in the degree of toxicity and intensity of symptoms, the variation depended on the method of administration and the type of HC used in the study. In most cases, inhalation exposures produced one or more of the changes observed in enzymes, hematology, carbohydrate metabolism, antagonistic muscle chronaxy

ratios, immunobiological responses, respiration, histology of vital organs, coproporphyrin elimination in urine, body weight gains, or livability. Often, growth, general behavior, and health remained unaffected, in spite of some of the above-mentioned changes. Extracts of benzene and its derivatives were carcinogenic.

The nerve gas that was responsible for the mass deaths of sheep was largely the result of improper management practices in the use of the gas.

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Chapter 13.—Hydrogen Sulfide

Hydrogen sulfide (H_2S) is a poisonous gas produced from the decomposition of animal matter containing sulfur. The gas is moderately soluble in water, which accounts for the presence of H_2S in marshes, swamps, and lagoons where decaying matter is ever present. Other sources of H_2S are oil-drilling fields, coal mines, volcanoes, and certain water (sulfur) springs. Although H_2S toxicity in the environment is not so critical as other air pollutants, the toxicity is best exemplified by the Poza Rica incident in 1950 (*10*): Poza Rica, a city located in Mexico, was the center of Mexico's leading oil-producing district and the site of field installation for natural gasoline manufacture, crude gas stabilization, gas desulfurization, sulfur recovery, and pressure maintenance. The daily capacity was 116,000,000 cubic feet of natural gas, which contained 3.14 percent H_2S, 15 percent CO_2, and 0.1 percent 0_2. Early in the morning of November 24, the escape of unburned H_2S into the windless, hazy atmosphere as a result of faulty mechanization produced illness among humans in the affected area—320 required hospitalization. Besides 22 human deaths, all canaries dies, and approximately 50 percent of other animals (chickens, geese, ducks, cattle, pigs, and dogs) died during the day. A brief review (*3*) of H_2S as one of several air pollutants affecting animals was presented.

EXPOSURE TO H_2S INHALATION IN THE FIELD

Swine

Heavy casualties among fattening pigs have occurred on several farms, especially in slatted-floor pens, while slurry tanks were being emptied (*1*, *8*, *9*). The composition of air during agitation of the stored slurry was analyzed on many farms and showed four major gases:carbon dioxide, methane, ammonia, and hydrogen sulfide. The concentrations of the first three gases did not reach the levels normally considered toxic to both pigs and man. However, the H_2S concentration, after a brief period of agitation, often reached an excess of 1,000 p.p.m. (1,391 mg./m.^{3}), which was higher than the accepted toxic level for pig and man.

Poultry

Two poultry farms were analyzed for H_2S content of agitated slurry (*9*). The level was in excess of 1,000 p.p.m. (1,391 mg./m.^{3}) at the manhole of the slurry tank on one farm and only 2 p.p.m. (3 mg./m.^{3}) on the other farm. No casualities occurred on the first farm because traps between the slurry tanks and poultry houses largely prevented the escape of gases back into the houses.

Cattle

Although the gases released during the agitation of cattle slurry were not examined, H_2S was believed to be the toxic gas for casualties among cattle in Sweden (*2*).

Laboratory Animals

A case history of H_2S poisoning of chinchillas was reported in 1959 (*5*). One evening at 6:45 p.m. the stove was fired with coal; at 10:45 p.m. the same evening, 16 of 18 chinchillas were dead. The two survivors showed no evidence of illness; they were located near a source a fresh air. The room reeked of an "acrid" odor. Autopsy ruled out CO poisoning. Instead of a cherry-red color, the tissues were cyanotic (purplish), and the lungs were gray and edematous; lead sulfide was present in blood and liver. The coal in the stove was believed to be the source of H_2S poisoning.

Unspecified Animals

H_2S poisoning in oil-drilling fields is an ever present hazard; the dosage required to kill most animals in a very short time ranged from 0.10 to 0.20 percent (1,391 to 2,781 mg./m.^{3}) in the air. As much as 8 to 10 percent (111,247 to 139,059 mg./m.^{3}) H_2S has been found in the gas of one particular Texas field, where in several cases, only one or two breaths caused almost instantaneous death to men. Many dead birds and animals (no information was given about the species) were found in the vicinity of the oil tank and wells (*14*).

EXPOSURE TO H_2S INHALATION IN THE LABORATORY

Swine

Swine were exposed to 50 to 1,200 p.p.m. (70 to 1,669 mg./m.^{3}) of H_2S for 1 second to around 4 hours (*11*). The results revealed that toxicity was related more to the H_2S concentration than to the length of time of exposure. No chronic effects were observed in pigs surviving exposures as great as 1,000 p.p.m. (1,391 mg./m.^{3}). Consequently, H_2S poisoning of domestic animals is considered unlikely under conditions other than those that have been responsible for such fatalities in man, that is, a sudden exposure to 500 p.p.m. (556 mg./m.^{3}) or more of H_2S.

Rabbits

Rabbits exposed to 50 p.p.m. (70 mg./m.^{3}) H_2S for 16 hours exhibited no symptoms; however, when the concentration was increased to a possible 1,000 p.p.m. (1,391 mg./m.^{3}) level by accident, tetanic spasm and unconsciousness occurred with one death 2 hours later. No aftereffects were observed in the survivors (*11*). In another study (*7*), rabbits were exposed to 0.1 mg./l. (100 mg./m.^{3}) of H_2S for 30 minutes daily for 7, 10, and 14 days. Then the animals were sacrificed, and their lungs excised and sectioned. The data showed a decrease in the following enzymes: acid phosphatase, alkaline phosphatase, adenosine triphosphatase, and desoxyribonuclease. Microscopic examination of lung tissue revealed deterioration. The effect of H_2S on connective tissue might differ in kind from its effect on lung tissue.

Humans

The physiological response of men exposed to the following concentrations by volume in air was as follows (*13*): 0.005 to 0.010 percent (70 to 139 mg./m.^{3}), slight conjunctivitis and irritation of respiratory tract after 1 hour of exposure; 0.02 to 0.03 percent (278 to 416 mg./m.^{3}) marked conjunctivitis and respiratory tract irritation after 1 hour of exposure; 0.05 to 0.07 percent (695 to 973 mg./m.^{3}) dangerous in $\frac{1}{2}$ to 1 hour; 0.07 to 0.10 percent (973 to 1,391 mg./m.^{3}), rapid unconsciousness, cessation of respiration, death due to asphyxiation; 0.10 to 0.20 percent (1,391 to 2,781 mg./m.^{3}), same as the previous level, with death in a few minutes. The first three and the last two concentrations represent the subacute and acute forms of H_2S poisoning, respectively. No evidence of chronic H_2S poisoning was found, primarily because the gas is rapidly oxidized in the blood to form nontoxic compounds, ultimately sulfates.

EXPOSURE TO H_2S INJECTION IN THE LABORATORY

Sheep, Cows, and Dogs

Sheep, cows, and dogs were given H_2S gas via rectum or stomach (*4*) to determine whether the toxic effects affected the respiratory center only or whether such action was incidental to an inhibition or some enzyme system affecting all body tissues. The data showed that the H_2S intoxication decreased the CO_2 content of blood, depressed the respiratory center, and caused death. CO_2 given intravenously or 10 percent carbogen inhalation increased the tolerance for, but did not abolish, the toxicity of H_2S. Artificial respiration prolonged life, but it did not prevent death of H_2S intoxicated animals.

MISCELLANEOUS

A maximum permissible concentration of 0.27 mg./m.^{3} of H_2S was recommended for cattle exposed to inhalation or ingestion of H_2S contaminated forage (*12*). H_2S was one of several air toxicants that lowered the immunobiological activity of rabbits, pigeons, man, and rodents against disease such as typhoid fever and anthrax (*6*).

RECOMMENDATIONS TO CONTROL H_2S TOXICOSIS

Animals should be removed from buildings during the active agitation of manure slurry tanks; effective traps between slurry tanks and pens should be airtight to prevent backing up of the gases. Raising of farm animals should not be permitted near oil-drilling fields.

SUMMARY

H_2S toxicosis represents the acute or subacute type of poisoning in animals. The hazard effects of H_2S on farm animals are considered unlikely under conditions other than those that have been responsible for such fatalities in man (400 p.p.m. (556 mg./m.^{3}) or more). Agitation of manure slurry tanks can increase the H_2S concentration in excess of 1,000 p.p.m. (1,391 mg./m.^{3}), a level that is fatal to pigs and man.

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Chapter 14.—Ions, Air

The atmosphere contains ions, also known as atoms bearing an electric charge. The ions are either positive or negative, both of which are necessary to permit an electrical charge. The degree of air ionization is dependent on several factors: electrolysis, displacement, double decomposition, conductivity, chemical activity (salts, acids, bases), and vapor-pressure, boiling-point, and freezing-point abnormalities.

Biological effects of air ions have been reviewed (*8*). Since a controversy exists in the literature about the significance of biological effects of air ions on animals, more well-controlled biological experiments are necessary to resolve the controversies. The emission of pollutants from various sources into the natural environment would undoubtedly influence ionization of the atmosphere because of the chemical properties of the pollutants. Very little is known about relations that might exist between the extent of air pollution and biological effects of air ions, especially with domestic animals.

EXPERIMENTS WITH DOMESTIC ANIMALS

Swine

Seven tests with pigs were conducted in three environmental chambers supplied with an excess of positive (+) ions, an excess of negative (−) ions, and equal quantities of (+) and (−) ions (control), respectively (*2*). The ions were produced via an ion generator. The results showed a wide variation among the tests: three tests showed no effects of ions on weight gains; one test, harmful effects of + ions; one test, harmful effects of − ions; one test, beneficial effects of − ions; one test, better weight gains for both + and − ions than for the control ion group. The weight differences during some of the tests were of such magnitude that the investigators found it difficult to dismiss the possibility that air ions could promote body weight gains of swine under certain conditions.

Poultry

Japanese quail

Nine trials were conducted with Japanese quail maintained in three environmental chambers supplied with excess + ions, excess − ions, and control ions, respectively, (*2*). Six trials were initiated at 1 day of age and lasted 28 days; the other three trials were initiated at 6 days of age and lasted through 28 days of age. In some trials the ions were supplied during the illuminated periods, and in others during the darkened periods of the 24-hour day. In all but one of the six trials, the growth rate was depressed by the − ions. In the other three trials, the results were inconsistent. Some evidence indicated similar growth rates with the + ions and control ions. One explanation for this finding may be attributed to similar + ion densities of the + ion and control ion groups, as measured by the ion counter. After termination of the nine trials, most of the quail were raised to sexual maturity in a natural environment; the results indicated no significant differences in all but one trial on the length of time required to reach 50 percent egg production. The one exception was the delay of sexual maturity by − ions provided only during darkness.

Chickens

Somewhere near Voronez, Russia, 1,000 chicks were used in a study—one-half as controls and the other half subjected to ionized air starting at 15 minutes per day with increments until a maximum of 2 hours per day was reached (*1*). The results indicated a 24 percent increase in body weights of ionized chicks, as compared with the controls, a lower mortality for ionized than for control chicks (8 vs. 18 percent), a lower evidence of avitaminosis in ionized than in control chicks (6 vs. 12 percent), a lower evidence of diarrhea (not pullorum) in ionized than in control chicks (10 vs. 100 percent), and greater liveliness in ionized than in control chicks. (Note: This article was translated for the benefit of the readers of the journal in which the article appeared; hence, some important data could have been inadvertently omitted. The avitaminosis and diarrhea syndromes suggest that perhaps ionization of air was being tested as a hygienic substitute for presumably substandard diets that might have produced avitaminosis and diarrhea. The translation also stated that studies would be continued to determine the effects of ionization on long-term growth, egg production, health status, and histology of embryos. None has been located in the literature survey so far.)

Cattle

Information on the physiological and pathological effects of high levels of NH_3 ions may be found in chapter 5.

EXPERIMENTS WITH LABORATORY ANIMALS

Hamsters

Hamsters were exposed to excess − ions (2,500 plus 250 + ions/cc. of air), excess + ions (2,600 plus 200 − ions/cc. of air), and control ions (75 to 250 − ions plus 100 to 350 + ions/cc. of air variable with weather conditions) for at least 60 days of the postnatal developmental period (*9*). The results of the T-test for significance indicated that the − ions significantly increased the weights of heart, kidney, testes, seminal vesicle, and epididymis as compared with controls. No significant differences were observed between the + ions and control ions.

Rats

Rats of two age groups (3 months and 14 months) were exposed to excess + ions (2.9×10^5 + ions/cc. of air), excess − ions (1.4×10^5 − ions/cc.) and control ions (600 + ions plus 600 − ions/cc.) (*3*). Criteria for evaluating behavioral effects were rate of learning of a water maze and performance in the maze after learning was complete. Half of the animals were subjected to a 60-v., 0.7 second electrical shock before maze trials. Results indicated that stress (electric shock) was not a necessary precondition for air ions to affect behavior. Learning of the maze was enhanced by both ion polarities, particularly by − ionized air; performance of older animals living in a − ionized atmosphere was significantly improved.

Various Animals

Research (*4*, *6*) with rabbits, mice, and rats exposed to excess + ions, excess − ions, and control ions indicated that + ions were harmful and reduced the efficiency of the respiratory tract (decreased ciliary activity and mucous flow rate, increased susceptibility of cilia to trauma, contracted posterior tracheal wall, dried epithelial surface). Excess − ions reversed the effects of + ions on ciliary activity, mucous flow rate, and contracture of tracheal wall. The data suggested that − ions contributed to the comfort and to the prevention of certain types of respiratory illness.

As is true with mice, rats, guinea pigs, and rabbits, + ions depressed ciliary activity of trachea of monkeys and man, while − ions increased the activity (*7*).

In rabbits, cigarette smoke produced a decrease in ciliary rate that was further decreased and made permanently decreased by + ions (*5*). The − ions reversed the effect of cigarette smoke on ciliary rate in a heavy atmosphere of cigarette smoke as well as in fresh clean air. The + ions required more carbon dioxide than present in the air to produce effects; whereas, − ions required more than a minimum of O_2 to take effect.

SUMMARY

Animals including man exposed to positive ions could become more susceptible to certain respiratory diseases because positive ions decrease ciliary activity of the trachea. Further evidence suggests a relation between ionization of the atmosphere and the biological effects of farm animals. More well-controlled biological experiments are needed to resolve the discrepancies on the biological effect of air ions on domestic animals, especially when exposed to air pollutants.

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Chapter 15.—Lead

Lead (Pb) compounds are present in numerous products such as paints, gasoline, storage batteries, metal containers, medicine, and orchard-spray formulas. Sources of Pb pollution for domestic animals are inhalation of Pb vapors or dust from industry, and ingestion of vegetation contaminated by industrial Pb dust, orchard-spray residues, or contact with metal containers or paints containing a Pb base. Pb toxicity could also occur through absorption of Pb in medication. Comprehensive reviews have been documented on Pb toxicity and absorption, mostly in humans and laboratory animals (*5, 14, 32*). However, some discussion on domestic animals was available (*1, 38, 39, 47*). Investigations with animals showed that Pb dust inhaled was far more dangerous and produced symptoms far earlier than by ingestion (*14, 32*). Even so, the literature review indicated the difficulty in many cases of drawing a line of demarcation between inhalation of Pb dust and ingestion of contaminated vegetation as a source of Pb poisoning in domestic animals near sources of Pb contamination.

EXPOSURE TO Pb INHALATION IN THE FIELD

A report published in 1840 contained proof that Pb was absorbed via the respiratory tract of a dog that died of Pb poisoning (*5*). Another investigator (*43*) reported three cases of Pb poisoning in individual dogs that had spent a great deal of time in the following environments, one in a railroad engine shed, a second one in an automobile garage, and the third one riding on the floor of an automobile—all dogs were exposed to ethyl Pb from gasoline fumes. The general symptoms were lethargy, poor appetite, sparse excretions, emaciation, albumin in urine, and tremors in the hindquarters with painful gait. In addition, stomatitis (inflammation of the mouth) developed in the first two dogs. Removal of the three dogs from the source of chronic Pb poisoning largely eliminated the symptoms. (Note: Although the investigators claimed that Pb was the causative agent of poisoning of the dogs, the possibility should not be overlooked that other components in gasoline could be more or less responsible for the poisoning symptoms.)

EXPOSURE TO Pb INHALATION OR INGESTION IN THE FIELD OR TO BOTH

Cattle

Cases of Pb poisoning occurred in cattle grazing on pasture contaminated by Pb emissions from factories (*10, 31, 34, 46*); however, no apparent injury was found in cattle near a smelter (*24*).

Symptoms in cattle exposed to Pb inhalation or ingestion of Pb-contaminated vegetation or both have been reported by several researchers (*10, 26, 28, 31, 34*). The acute symptoms included one or more of the following: loss of appetite, constipation, delirium, salivation, extreme thirst, reduced milk yield. Those of chronic Pb poisoning were altered metabolism, emaciation, cachexia, enteritis, muscular twitches, nervous disorders, colic, swollen joints, pale muscles, chewing atony, diarrhea, bellowing stupor, incoordination, lethargy, rough coats, reduced erythrocyte, thrombocyte, and hemoglobin values, and convulsions. Sudden death sometimes occurred. The pathological findings indicated hyperemia of the rumen and intestinal linings and degeneration of liver (*10*), and degenerative esoinophilic meningoencephalitis (*31*).

In contaminated areas, the Pb content of hay and silage was 4 and 67 to 139 p.p.m. respectively, as contrasted with 0.6 and 0 to 1.8 p.p.m. for control hay and silage, respectively; that of control and contaminated grains was 0.4 and 5.5 p.p.m., respectively (*41*). Beet pulp kept in metal containers was a primary source of Pb poisoning in a number of cases (*35*). The Pb determinations of three samples of beet pulp removed from the middle of the container, removed unscraped, and removed scraped from the wall of the container were 20 mg., 1.2 g., and 1.4 g./kg. of beet pulp, respectively. The cows fed the unscraped beet pulp and beet pulp scraped from the vicinity of the container wall succumbed to Pb toxicosis. The clinical manifestations included, in addition to the symptoms described in the preceding paragraph, grinding of teeth, visual defects, gastrointestinal disturbances, dry blackish feces, acute nephritis, and bluish discoloration on lower gums after 7 days of exposure.

In chronic Pb poisoning, cattle could consume 1 to 2 g. of Pb daily for over 2 years without ill effects; in diagnosis, kidneys as well as blood and feces, should be analyzed for evidence of Pb poisoning (*2*). Calves fed for 3 months hay that contained 22 p.p.m. Pb remained normal in every respect (*6*). A value of 0.15 mg./m.^{3} of Pb was considered the maximum permissible atmospheric concentration for cattle (*44*).

Horses

Chronic Pb intoxication was reported among horses in the vicinity of Pb forges (*6*, *25*, *27*, *34*). Most of the cases occurred in late fall or early winter, because the Pb content of grass and hay was much higher in winter (1,280 to 2,270 p.p.m.) than in summer (270 to 980 p.p.m.) (*6*). In another area pasture grass near a Pb smelter contained from 89 to 312 p.p.m. Pb (*25*). In the vicinity of two forges, the forage dusts contained 16.9 and 44.8 percent Pb in addition to other minerals (*27*).

The principal symptoms of acute poisoning in horses were salivation, affected respiration (bronchial catarrh, pharyngitis), colic, dilation of eye pupils and nostrils, anemia, delirium, or paralysis. In chronic cases, the symptoms included pulmonary gangrene, emphysema, cough, bronchitis, roaring, pallid mucous membranes, muscular weakness, stiffness, articular lesions including synovitis, emaciation, partial paralysis of the larynx, dry and harsh coats, chronic nephritis, hypertonia, delirium, melancholy, abortion and subsequent sterility, constipation alternating with diarrhea, coma, or suffocation from slightest exertion (*6*, *7*, *16*, *24*, *25*, *26*, *27*, *34*). Although changes in blood and albumin were observed by one investigator (*7*), no hematological changes were noted by several coinvestigators (*25*).

The Pb content of various organs from horses that died from Pb toxicity was: 143, 27, 48, 85, and 70 p.p.m. for liver, kidneys, stomach, cecum, and colon, respectively (*46*); 3.9 to 7.3 mg./100 p.p.m. for liver (*25*); excess of 2 p.p.m. for liver (*27*).

In the 1920's and 1930's, when lead arsenate was commonly used as an orchard spray, Pb poisoning was common among farm animals (*33*). Horses were heard to choke, followed by roaring and paralysis when exercised. Laryngeal hemiplegia, with the hanging of the lower lip, was the predominating symptom. More losses occurred in the fall and winter than in summer because of closer grazing.

Sheep and Goats

Goats fed hay containing 22 p.p.m. Pb for a 3-month period grew normally (*6*). Sheep and goats, though sensitive to Pb toxicity, were more resistant than cows; one variety of sheep (Merino) was believed to be more susceptible to the effects of Pb than the regional strain or the Merino-regional hybrids (*17*). Sheep were not affected in an area contaminated by Pb emissions (*24*).

If given a choice, sheep preferred the contaminated pastures to noncontaminated pastures in grazing areas near a Pb mining region (*12*). Shepherds for over 50 years have tried to herd the sheep away from contaminated areas as much as possible; the incidence of Pb toxicosis appeared to be related to the efficiency of the shepherds in keeping the sheep away from contaminated areas. The clinical features of the disease, osteoporosis, were unthriftiness, fragile bones, lameness, posterior paralysis; the pathological findings included kidney lesions, basophilic stippling of red erythrocytes, high Zn levels in blood and tissues, and generalized deficiency of osteoid tissue.

Spring lambs exhibited paralysis of the respiratory tract and anemia during the months of February, March, and April when the wind was from the north and southeast (*37*). Later, weakness, loss of appetite, and death were observed. Adult sheep were unaffected. The grass was believed to contain from 86 to 220 mg. percent of Pb, on the basis of analysis of rooftop snow exposed to the Pb emissions from a smelter.

Swine

Chronic forms of Pb poisoning were rarely observed in this species. Cases of Pb poisoning appeared on different farms with different breeds of different ages within the vicinity of the industrial plant, especially under high humidity conditions in the absence of wind (*18*). The gravity of symptoms depended on the age (younger animals being more sensitive) and the quantity of absorbed Pb. Data suggested that Pb absorption via the gastrointestinal tract was less than via inhalation. The symptoms that appeared several days after exposure to Pb emissions included loss of appetite, blackish diarrhea with a putrid odor, extreme salivation, rapid respiration and increased excitability by hitting against obstacles. The pathological symptoms after death revealed hemorrhage in the intestine; hypertrophied, degenerated, pale liver covered with tiny necrotic spots; congested kidneys; and slightly degenerated heart with hemorrhage. Conversely, in one study (*24*) no apparent injury was observed in swine exposed to Pb emissions in the air or on vegetation or both.

Poultry

The only specific information was that 26, 14, and 64 p.p.m. Pb were found in the gizzard, liver, and kidneys, respectively, of a hen that died of Pb poisoning (*6*).

Page 1224 of the 1942 Yearbook of Agriculture (*45*) stated, ". . . Pb deposits released from smelters have been known to result in considerable losses in waterfowl." No references were given to support this statement. (Note: The literature survey revealed several references on poisoning of waterfowl from lead shot via the hunters' guns or via ingestion; none could be found about Pb emissions from smelters.)

Rabbits

A definitely greater accumulation of Pb occurred in bones, liver, and muscles of rabbits exposed to herbage grown in Pb-contaminated areas than in nonexposed rabbits; the respiratory uptake was lower in exposed than in nonexposed animals (*29*).

Species Differences

Two marked differences were observed between cattle and horses: Pb toxicity in cattle came chiefly from ingestion of contaminated pasture, but horses became poisoned more from drinking contaminated river water (*19*). Why this water was not so dangerous to cattle as to horses was theorized as follows: Cattle enter the river daintily, hardly disturbing the water and drink the clean water; horses, on the other hand, splash into the water and paw the riverbed making it "soupy" before drinking. The soupy water contained the deadly Pb silt. In cattle, the symptoms were choking, alimentary disturbances, dullness, partial or complete blindness, great excitability, and intermittent fits; death ensued. In horses the symptoms were more or less subacute and chronic: dyspnea, roaring, labial paralysis, dropped ears, and only one case of blue line in the mouth.

Species difference was also observed on two farms, one (A) across the highway from the smelter and the other (B) 1 mile north of the smelter (*22*). On farm A, seven out of 20 milking cows and one of two draft horses died within a 2-month period; on farm B, six out of eight ponies died during the winter and early spring, while none of the four cows were affected. The Pb concentration in blood of normal and poisoned cows in this area was 0.10 p.p.m. and 0.35 to 2.4 p.p.m., respectively; that of normal and poisoned horses was 0.04 p.p.m. and 2.0 to 4.0 p.p.m., respectively. Analyses of pasture grasses, alfalfa, and clover hay grown in the smelter area and corn silage produced locally contained from 148 to 3,200 p.p.m. Pb. Sudden death with vague signs of emaciation and depression occurred in cattle; and sudden death, convulsions, dyspnea, and roaring after mild exercise, in horses and ponies.

One study (*20*) indicated that horses could stand 10 times the dose necessary to kill a cow. Conversely, in another study (*24*) it was found that horses were affected by Pb emissions, whereas cattle, sheep, and swine remained normal.

Humans

People living in the areas where ponies and cattle were poisoned on farms A and B, did not carry abnormal accumulations of Pb (*22*). In another area where spring lambs but not adult sheep were affected, the inhabitants complained of laryngitis, tonsilitis, and bronchitis, which might have stemmed from SO_2 as well as from Pb (*37*).

EXPOSURE TO Pb INHALATION IN THE LABORATORY

Cats

The quantity of inhaled Pb dust required to produce poisoning symptoms was 0.0007 g./1. (700 mg./m.^{3}) after 12 inhalations of 1 hour each for 37 days or 0.0001 g./day in a 120-day period (low sublethal chronic level) (*32*). The symptoms were: a slight increase in body weight from 1 to 3 weeks, followed by a progressive diminution in weight; wasting of spinal muscles; general paralysis of body, especially hindquarters; constipation; and hemorrhage of organs. Since Pb was much more commonly present in feces than in urine of poisoned cats, the feces should be analyzed for Pb. Chronic Pb intoxication might occur if the atmosphere contained 0.2 mg. Pb/m.^{3}

Rabbits

Chronic exposure to PbO concentration of 10 g./m.^{3} (10,000 mg./m.^{3}) daily for 6 hours over a period of 6½ months increased the urine-eliminated coproporphyrin up to 10.6 g./day. Exposure of similar duration to 3.9 g./m.^{3} (3,900 mg./m.^{3}) of PbO had no effect (*21*).

Species Differences

In one study (*42*), monkeys, dogs, rabbits, guinea pigs, and pigeons were exposed for either 3 hours/day/6 days a week or 6 hours/day/5½ days a week to 0.0004 mg. Pb/ft.^{3} (0.000088 mg./m.^{3}) for about 20 weeks, followed by 0.0041 mg. Pb/ft.^{3} (0.00091 mg./m.^{3}) for 13 weeks. The source of Pb was from ethyl gasoline. With one or two exceptions, no differences existed between the exposed and nonexposed animals.

In another study (*42*), when the Pb concentration was increased to 0.40 mg./ft.^{3} (0.0088 mg./m.^{3}), Pb storage became apparent and accumulated in greater quantities as time progressed. The pathological findings included liver degeneration in guinea pigs and pigeons, kidney degeneration in dogs and rabbits, and none in monkeys. Hematological values, general health, body weight, and growth remained unaffected in all species with one exception: pigeons lost weight toward termination of the 13-month study.

EXPOSURE TO Pb INGESTION IN THE LABORATORY

Sheep

When sheep were fed varying levels of Pb per day along with hay and oats in some cases, the data (*8*) indicated: (a) The fecal Pb was largely excreted as phosphate or sulfide and consisted largely of unabsorbed food Pb; (b) within the range of intake of 2 mg. to 40 g. Pb, absorption was very small; (c) urinary excretion of Pb was dependent on Pb intake but did not exceed 0.8 mg. daily, on low intakes of Pb (2 mg.) the urinary Pb excretion was of the same order of magnitude as that in the normal human; (d) Pb excretion in ewe milk was rather high when ewes were fed dietary Pb; (e) bile was the major channel of Pb excretion when large quantities of Pb were fed; (f) no Pb retention was observed in sheep fed very low levels of Pb; but higher levels resulted in Pb retention by tissues—this differed markedly from that with mice, rats, and humans.

Pb intoxication (1 mg. per kg. body weight per day) induced abortion in sheep if ingested during pregnancy, especially among ewes in poor condition (*3*). Further studies suggested that the herbage contaminated with Pb soil dust could result in at least 130 p.p.m. Pb being consumed. However, Pb in this form was relatively nontoxic, and the Pb content of sheep blood showed no real danger of plumbism; hence, there was little or no evidence of chronic Pb posioning in sheep.

Cattle Versus Sheep

In many cases, acute poisoning symptoms differed for cattle and sheep (*3*). Calves exhibited dullness, abdominal pain, constipation sometimes followed by diarrhea, excitability, muscular spasms and tetany, followed by death; the lethal dose was 0.2 to 0.4 g. of Pb/kg. body weight, whereas 6 mg./kg. of body weight was tolerated as long as 3 years. In sheep, a slight rise in body temperature, anorexia, reduced water consumption, dullness, lethargy, ataxia of hindquarters, and no evidence of abdominal pain were observed. Pathological findings showed very little changes in calves, as contrasted with extensive inflammation of the intestine and damage to kidneys in sheep.

Cattle Versus Horses

Feeding trials showed that 60 to 70 g. of PbO administered in small doses produced death in cattle; whereas, 135 g. fed to one horse for 2 months did not produce any damages (*34*).

Chickens and Rabbits

In experiments (*15*) with chickens, White Leghorn and Houdan sires were mated with White Leghorn hens to produce progeny identifiable with characteristics associated with the sire. The Leghorn sires were poisoned via Pb acetate in capsules (quantity unknown), and the Houdan sires and all hens were not poisoned. The fertility was 73 and 58 percent, and the hatchability of fertile eggs was 72 and 82 percent, respectively, for the poisoned and nonpoisoned sires. The mortality the first 3 weeks of life was 16 and 0 percent for the progeny of the poisoned and nonpoisoned sires, respectively; this suggests that Pb-poisoned males resulted in distinctly lower average vitality in progeny. (Note: The experimental design was poorly planned because poisoned males of one breed cannot be compared with nonpoisoned males of another breed. The difference in the vitality of progeny is really a result of hybrid vigor rather than Pb poisoning.)

Similar studies with Dutch and albino rabbits indicated that the offspring of Pb-poisoned sires were lower in vitality and smaller than those of nonpoisoned sires (*15*).

COMPARISON OF Pb INGESTION AND INJECTION IN THE LABORATORY

Two methods of administration (oral and injection) of Pb in sheep and rabbits resulted in differential distribution of Pb in tissues (*9*). Generally speaking, Pb given intravenously as the acetate followed the distribution of the reticuloendothelial cells of the body; when given by mouth, most of the Pb was deposited in the skeleton with very high concentrations in the kidney. Over a long period the Pb concentration remained high in the kidney after injection, presumably because Pb released from other tissues in small quantities was taken up by the kidney in an attempt to excrete Pb in the urine.

PHYSIOLOGICAL ASPECTS OF Pb

Metallothionein, a protein isolated from liver and kidney of Pb-poisoned animals (horses, rabbits), binds Pb in vivo and also in vitro; Pb was found to inhibit a number of enzymes and alter the normal biochemical actions within the body, and protection could be afforded by coenzymes and substrates (*48*). Lead accumulated in the liver is toxically inactive; however, whenever the Pb enters the bloodstream, symptoms of Pb poisoning occur (*41*).

TOLERANCE LEVELS

Toxic doses are 50 to 100 g. for ruminants, 500 to 700 g. for horses, 20 to 25 g. for sheep and goats, and 10 to 20 g. for pigs and dogs. Young animals are more sensitive than adults; sex is not a significant factor (*7*). Animals raised in contaminated areas tended to absorb increased quantities of Pb in contrast to older animals brought into such areas (*41*). The intensity of Pb poisoning was not always related to the amount of Pb ingested (*7*) or to the Pb content in the liver (*41*).

DIAGNOSTIC AND ANALYTICAL METHODS

The methods for determining Pb in air and in biological materials are adequately, if not thoroughly, described with 95 references being cited (*4*). A new method was described in which Pb detection in bovine blood and liver was made possible by a simplified, clear color differentiation technique (*23*). Although the liver is the common organ for diagnosis of Pb toxicity, the following biological materials should be analyzed for Pb besides the liver: kidneys (*2*), blood samples (*41*), and feces (*32*).

Difficulty in diagnosis increases with increased time lapse after ingestion of Pb (*7*). Since Pb distribution in livers may not be necessarily homogenous, samples should be taken from four places of the same liver and homogenated for Pb analysis (*40*).

MISCELLANEOUS

Contents of Pb in Various Products

Organs

The Pb content (p.p.m.) of fresh liver and kidney tissue from normal sheep and cows was 0.3 to 1.5; that of blood varied from 0.129 to 0.140 for normal calves, goats, sheep, and horses (*2*). The Pb concentration in blood was about 0.10 p.p.m. and probably 0.04 p.p.m. for healthy cows and horses, respectively, as contrasted with 0.35 to 2.4 and 2.0 to 4.0 p.p.m. for poisoned cows and horses, respectively (*22*). Although 4 p.p.m. Pb in animal livers is always a positive indicator of Pb toxicity, massive poisoning has occurred in animals whose livers contained less than 4 p.p.m. Pb (*41*).

Milk

The Pb concentration in milk was linearly related to the concentration in blood cells at a ratio Pb cells/Pb milk of 23 (*22*).

The Pb content of market milk samples obtained on a quarterly basis from 59 cities throughout the United States ranged from 0.023 to 0.079 p.p.m. with a national weighted average of 0.049 p.p.m. (*36*). The variation between cities was not significant. Analysis of 76 individual cow milk samples in three States showed a variation of Pb content of 0.0009 to 0.212 p.p.m., with an average of 0.047 p.p.m.

Soil

Surface soil analysis of exposed and unexposed areas in the vicinity of a smelter indicated 15.2 and 2.9 p.p.m. Pb, respectively, which was directly related to Pb toxicosis in horses (*24*). On one farm where 33 percent of the cattle died from Pb poisoning, the top inch of soil contained an excess of 1,000 p.p.m. Pb as a result of Pb emissions from a smelter (*22*).

Vegetation along highways

In the Denver area (*13*) the Pb content of grass samples obtained at the major highway intersections where the traffic was heavy, within 5 feet of the highways, and 500 to 1,000 feet from the highways was 3,000, 100 to 700, and less than 50 p.p.m. in ash, respectively; other minerals were also present. Homegrown vegetables in the New York and Maryland areas showed an average of 80 to 115 p.p.m. Pb within 25 feet of a paved road as contrasted with an average of 20 p.p.m. at least 500 feet away from the same road; the range was 10 to 500 and less than 10 to 200 p.p.m. for the two distances, respectively. (Note: No information is available on the performance of domestic animals ingesting Pb-contaminated vegetation near highways.)

Resistance to Disease

Data on rabbits showed that in chronic Pb poisoning the immunologic reactivity of the rabbit to typhoid vaccine was considerably reduced; this reduction was more pronounced in rabbits subjected to Pb intoxication before rather than after the initiation of immunization injections (*30*).

ALLEVIATORS

Of all the alleviators used to counteract the toxic effects of Pb, chelating agents such as EDTA (ethylenediaminetetraacetic acid) were most commonly used. The EDTA containing Ca (calcium) complexes with Pb inside the body of the poisoned animal in such a manner that Pb replaces Ca in the molecule, then the Ca is released, and the resulting Pb-EDTA becomes nonionizable and is readily excreted via feces. The EDTA treatment has proved successful (*16*, *18*, *25*, *28*, *48*); conversely, this treatment can be hazardous especially in chronic cases (*17*, *22*). EDTA was also known to counteract the effects of Pb on enzyme inhibition in horses and rabbits (*48*).

Other alleviators used were: Antoxol which consisted of 200 mg. of 2.3 dimercaptopropanol plus 400 mg. of benzylbenzyate in vegetable oil (*43*), 1 percent sodium calcitetracemate-glucose solution

(*35*), a Ca-Mg solution (*46*), morphine and chloral hydrate (*7*), injection of ample Ca, followed by a low intake of Ca, acids and their NH_3 salts (*5*), and diets rich in minerals (Ca, P, Zn), vitamins (ascorbic acid, thiamine), and protein (*11, 12, 17, 28*) but not diets rich in fats (*11*).

Tracheotomy provided temporary relief in horses (*26*). The possible correction of the smelter-emitting techniques might have reduced to a minimum the number of subsequent complaints received from animal owners in one area (*24*).

SUMMARY

The data on lead (Pb) toxicity of domestic animals reveal a large degree of variation in susceptibility within and between species of animals exposed to Pb via inhalation or ingestion or both. No definite trend on the toxic levels of Pb was apparent. Toxicity of Pb appeared to be greater via inhalation than ingestion. Some of the symptoms of Pb toxicity (plumbism) were harsh, dry coats, loss of appetite, emaciation, constipation or diarrhea or both, excessive salivation, muscular spasm, and frequently, paralysis of hindquarters, excitability affected respiration, roaring in horses, altered erythrocyte, thrombocyte, and hemoglobin values, hemorrhage of organs, reduced milk yield, and abortion and poor reproductive efficiency in some cases. The blue line on the gum, characteristic of Pb poisoning, especially in horses, was an infrequent observation.

The toxic doses are 50 to 100 g. for ruminants, 500 to 700 g. for horses, 20 to 25 g. for sheep and goats, and 10 to 20 g. for pigs and dogs. Younger animals were more sensitive than older animals; sex was not a significant factor; a breed difference in sheep was observed. Difficulty in diagnosis increased with increased time lapse after ingestion of Pb. In the diagnosis of Pb toxicosis, kidneys, liver, blood, and feces should be analyzed for Pb content. Variation in the Pb content of animal tissues, forage, soil, air, and water can become misleading in the diagnosis of Pb toxicity, because the intensity of Pb intoxication is not necessarily related to the amount of Pb ingested or to the Pb content in the liver.

The use of chelating agents (EDTA) and diets highly fortified with certain minerals (calcium, phosphorus, zinc), certain vitamins (ascorbic acid, thiamine), and protein-rich supplements appears to have some therapeutic value in counteracting effects of Pb poisoning.

The fact that the Pb content of vegetation grown along major highways was high should be of some concern from the standpoint of air pollution. Nevertheless, no information on theing estion of contaminated vegetation by domestic animals grazing near the highways has been documented.

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Chapter 16.—Manganese

Manganese (Mn) is one of the few metals that has been emitted into the atmosphere in quantities probably too small to be considered significant from the health viewpoint. However, complaints from farmers concerning loss of sheep and cattle prompted an investigation (*1*). High concentrations of Mn, as well as lead (Pb) and copper (Cu), were found in the carcasses of dead animals. The source of these three minerals was the nearby coke-oven industry.

A value of 6 mg./m.^{3} of MnO_2 was recommended as a maximum permissible concentration in the atmosphere for cattle grazing in the vicinity of large industrial plants (*3*).

The passage and deposition of Mn in the body were determined by exposing rabbits to 0.05 mg./l. (50 mg./m.^{3}) of aerosolized MnO_2 via inhalation for 1 hour/day for 6 months (*2*). The results indicated that the chronically inhaled Mn aerosol accumulated in the blood and in the cerebrum; the Mn passed from the lungs in an insoluble form into the blood. The Mn content in milligram percent was 0.3, 0.43, and 0.3 for blood, lungs, and cerebella, respectively, for exposed rabbits as contrasted with 0.05, 0.2, and 0.2, respectively, for controls. No differences were observed in other organs. No mention was made in the report that inhalation of 50 mg./m.^{3} of MnO_2 was harmful to rabbits.

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Chapter 17.—Mercury

Mercury (Hg) occurs as a free metal and as mercuric sulfide (cinnabar); the mercury ore is roasted, sulfur dioxide escapes, and the mercury vapor is condensed in long, tortuous flues. The literature survey has revealed several cases of toxicity of Hg vapors among farm animals.

EXPOSURE TO Hg VAPORS IN THE FIELD

Cattle

One month before the illness of a herd of 23 cows, one cow had been treated with an Hg ointment for mastitis. When the illness occurred, the symptoms were coughing, nasal discharge, fever, emaciation, skin and mouth lesions, and multiple hemorrhages in the mucous membrane of nose and mouth (*3*). Autopsy was performed on four of the eight that died in the herd; the following pathological symptoms were revealed: parenchymatous degeneration in liver, kidneys, and myocardium; gastroenteritis; and interstitial nephritis. Since Hg poisoning was suspected, the organs were analyzed for Hg content. The results revealed 100 to 1,000 times more Hg found in kidneys, liver, and spleen than should be normally present.

Sheep and Cattle

In one barn two sheep, one cow, and one calf were exposed to the one horse that was treated with an Hg ointment (*4*). Symptoms among the sheep and calf began to appear after the fifth or sixth day after the initial treatment; the symptoms were coughing, dyspnea, anorexia, lethargy, and loss of appetite. Both sheep died 3 weeks later; their pathological findings included nephrosis, enteritis, hemorrhage, hydropericardia, hyperemia, and edema of lungs, and high Hg content in liver and kidneys. The symptoms in the calf and cow were less pronounced than in the sheep, even though the Hg content in cow urine was very high (0.23 p.p.m.). The Hg concentration of the barn air under poor ventilatory conditions ranged from 1 to 2 mg./m.^{3}, as contrasted with 0.6 to 0.7 under adequate ventilation. Hence, adequate ventilation is important in minimizing Hg toxicity in the barn air as a result of Hg ointment therapy.

EXPOSURE TO Hg VAPORS IN THE LABORATORY

Pigeons motivated by food deprivation were trained to a multiple FR–60 FI–15 schedule of reinforcement (a method of teaching pigeons how to peck certain lights for food) (*1*). After stable behavior was established, eight birds were exposed to 17 mg./m.^{3} of Hg vapor for 2 hours daily, 5 days a week. The termination of Hg exposure for individual birds was determined by one of two endpoints: (a) Complete failure of bird to respond or markedly lowered rate of responding for 1 to 3 days, or (b) death. The results indicated marked changes in behavior, as measured by a decrease in the average rate of responding and spontaneous tremors in the head, neck, and wings; no histopathological changes were observed. The controls showed no appreciable change in behavior throughout the study; return of exposed pigeons to normal air restored the normal behavior patterns.

In another study (*2*), trained pigeons exposed to 0.1 mg./m.^{3} of Hg vapor for 6 hours daily, 5 days a week for 20 weeks showed no changes in behavioral, histological, or gross patterns attributed to Hg poisoning.

SUMMARY

Hg vapors can be toxic to farm animals maintained in poorly ventilated barns. The macrosymptoms included coughing, dyspnea, nasal discharge, hemorrhage, loss of appetite; the pathological findings revealed nephrosis, degeneration in liver, kidneys, and lungs, and hydropericardia. Behavioral patterns can be affected by high but not low concentrations of Hg vapors in pigeons in laboratory studies.

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Chapter 18.—Molybdenum

Molybdenum (Mo) has been used as a catalyst in many industrial plants where special steel and other metal alloys are manufactured. Contamination of vegetation grown in the vicinity of such industries has resulted in Mo poisoning of animals, much more so in foreign countries than in the United States (*15, 16*). Mo toxicity in domestic animals was briefly reviewed (*1*); no information could be found on the effect of Mo inhalation on the performance of farm animals in the field.

EXPOSURE TO Mo INGESTION IN THE FIELD

Cattle

Symptoms

In areas where the source of Mo poisoning, formerly known as "teartness," was not revealed, Mo-contaminated vegetation (20 to 100 p.p.m.) caused diarrhea, emaciation, reduced milk yields, and death in cattle (*2, 8, 9*). In one case, the hide color was affected: Red Devon cattle turned a dirty yellow, and black cows became rusty in color.

Cattle on farms located in the vicinity of metallic factories exhibited symptoms of Mo poisoning similar to those described in the preceding paragraph. Other symptoms included: enteritis, low copper (Cu) levels and high Mo levels in the blood, and stiffness of legs and backs; the pathological findings in one dead cow showed hyperemia in the jejunal mucous membrane and fatty liver (*3, 10, 12, 14*). The Mo content of contaminated pasture near factories contained up to 231 p.p.m. of dry substance, as contrasted with 1.5 p.p.m. for uncontaminated pasture; the blood Mo level was 25 times greater for cattle grazing on contaminated pastures than that for cattle grazing on uncontaminated pastures (*12*).

Alleviators

Administration of copper sulfate ($CuSO_4$) via ingestion, drench, or injection completely counteracted molybdenosis, even if the animals remained on the contaminated pasture (*2, 3, 9, 10, 12, 14*). The levels of $CuSO_4$ used in the feed ranged from 2 g./cow/day to 1 g./100 lb. of body weight (*3, 9, 10*). The drench method called for a daily dose of 2 g./cow or 1 g./calf or 5 g./7 days/cow (*3, 9*); the injection therapy included 120 or 500 mg. per cow (*10, 12*).

Scrubbers fitted to the flues of an aluminum-alloy factory in the autumn eliminated the symptoms of industrial molybdenosis among cattle the following summer (*14*). After the shutdown of another factory, observations continued on the cattle revealed that several months later the Mo values returned to the normal range as found in unaffected areas (*11*).

Horses

Horses exposed to industrial molybdenosis remained unaffected on farms where cattle were affected, even though very high blood Mo levels were found in the horses on one farm (*8, 12*).

EXPOSURE TO Mo INGESTION IN THE LABORATORY

Poultry

Growth of chicks and poults was depressed by 25 percent by the addition of 300 p.p.m. Mo to their rations (*13*). The addition of Cu (up to 400 p.p.m.) to high Mo-supplemented rations caused slightly improved growth. No evidence of diarrhea or anemia, as typical of cattle and sheep exposed to high Mo, was observed; neither was any evidence of depigmentation, as typical of red or black cattle exposed to Mo, observed with bronze feathers of poults fed Mo.

Sheep

A relation between Mo, Cu, and sulfate was demonstrated in feeding trials. High Mo-supplemented diets (10 or 100 mg./day) significantly reduced the Cu concentration in the liver of sheep, especially in the presence of inorganic sulfate (*5, 6*). However, inorganic sulfate did not permit the buildup of Mo in the blood as did sulfate-low diets in the presence of high Mo levels in the diet (*4*). This finding is important because chaffed lucerne hay and oaten hay contain a high and a low inorganic sulfate content, respectively; hence, the oaten hay did not affect the Cu concentration in the liver of sheep fed high Mo levels (*4*, *5*).

EXPOSURE TO Mo INHALATION IN THE LABORATORY

The inhalation of various Mo compounds as a dust or as fumes at the concentration of 5 mg. Mo/ft.^{3} (1.1 mg./m.^{3}) proved injurious (*7*). No fatalities occured in animals exposed to Mo fumes for twenty-five 1-hour exposures at an average concentration of 1.5 mg./ft.^{3} (0.33 mg./m.^{3}). The pathological changes were alveolar and bronchial exudates, necrosis of kidneys and livers, and some bronchopneumonia. Urinalysis is a good indication of Mo contamination in the atmosphere.

SUMMARY

Industrial molybdenosis is not so prevalent in the United States as in foreign countries. Horses were apparently more resistant than cattle to molybdenum (Mo) poisoning from ingestion of contaminated vegetation. Diarrhea, emaciation, reduced milk yields, low copper (Cu) and high Mo levels in the blood, stiffness of legs and backs, change in hide color, and death were observed. Treatment with copper sulfate via ingestion, drench, or injection eliminated the symptoms of industrial molybdenosis, even if the animals remained on contaminated pasture.

Feeding trials with chicks and poults indicated Mo toxicosis with respect to growth but not to diarrhea or anemia, typical of cattle, or to depigmentation of bronze poult feathers, as reported with red and black cows. A relation between Mo, Cu, and inorganic sulfate was demonstrated with sheep.

Inhalation of Mo dust or fumes proved injurious to guinea pigs from the clinical and histopathological aspects. Repeated exposures to low levels produced no fatalities.

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Chapter 19.—Nitrogen Oxides

Nitrogen oxides (NO, NO_2) are of some concern because of their presence in automobile exhausts and industrial emissions and because nitrates are extensively used as fertilizers on farmland. The nitrates normally utilized by plants are converted into amino acids and protein in the presence of energy from sunlight. However, in some unusual cases, nitrates might accumulate in the plants and produce nitrous acid (HNO_2) under intense heat (as from fermentation of plants in silos); the HNO_2 then develops into nitric acid (HNO_3), then nitrogen oxide (NO) and nitrogen dioxide (NO_2), and finally nitrogen tetroxide (N_2O_4). The biological effects of some of these nitrogen oxides that are poisonous to man and animals have been reviewed (*5, 23, 24*). The nitrogen oxide safety limit should not exceed 0.5 to 1 p.p.m. (0.6 to 1.2 mg./m.^{3}) (*5*). According to the literature survey, all cases of poisoning by nitrogen oxides among farm animals originated in silos.

EXPOSURE TO NITROGEN OXIDE INHALATION IN THE FIELD

Reports have been received from various veterinarians about the lethal effects of a yellow gas seeping from the bottom of silos on different farms. Animals such as chickens, pigs, calves, and even flies that passed by the silo chute door from one side to the other died instantly from the seeping gas identified as NO_2 (*1, 2, 3, 6, 17, 19*). Deaths among farmers working in or near the silos were common, the malady being diagnosed as "silo-fillers' disease" (*2, 3, 6*).

The yellow gas was so strong that rope and burlap bags left in the silo room were completely disintegrated (*19*). When 2-year-old heifers were turned outdoors after a coughing spell, panting became heavy in spite of fresh air, and death occurred in 2 hours (*1*). Every time the silo chute door was opened for feeding purposes, cattle within 20 feet of the chute door began coughing and showed an increase in the respiratory and pulse rates (*17*). As the symptoms progressed, the cows went off feed and developed high temperature and hypersalivation; breathing was by mouth with the tongue protruded. Cows kept outdoors and given the freshly ensilaged corn fodder obtained from the gas-filled silo began to exhibit the symptoms typical of "silo-fillers' disease" in man. When the silage was removed from the premises, the syndrome cleared up in 2 weeks.

Analysis of the yellow gas in the silos revealed an NO_2 concentration of 151 p.p.m. (284 mg./m.^{3}) (*2*) and 115 p.p.m. (216 mg./m.^{3}) (*3*). The maximum safe concentration was 25 p.p.m. (47 mg./m.^{3}) (*2*); however, 15 to 25 p.p.m. (28.2 to 47 mg./m.^{3}) were considered hazardous (*3*).

The factors responsible for the high nitrate of plants used for silage are: excessive fertilizing of pasture, drought, low light intensity, species and variety of plant (*6*), and immaturity of plant at time of ensilage (*2, 6, 19*).

The physiological and pathological findings revealed methemoglobinemia, dilation of blood vessels, and decrease in blood pressure. These symptoms appeared to affect the brain first (*6*). Methemoglobinemia in poisoned animals is not due to inhalation of nitrogen oxides but due to a reduction of nitrates to nitrites by bacterial action in the rumen; the nitrites already absorbed into the blood oxidize the ferrous heme or hemoglobin to the ferric heme producing methemoglobin.

Evidence indicated that NO and NO_2 lowered the defense powers of rabbits, pigeons, man, and rodents against diseases such as typhoid fever and anthrax (*14*).

EXPOSURE TO NITROGEN OXIDE INHALATION IN THE LABORATORY

Rabbits

Rabbits were continuously exposed to 8 to 12 p.p.m. (15 to 23 mg./m.^{3}) NO_2 for approximately 3 months (*9, 10, 16*). During the first 12 weeks of exposure, 50 to 60 percent of the rabbits died. The pathological studies showed pulmonary congestion, edema, bronchiolitis, and destructive changes in the alveolar walls; the most consistent and marked abnormality was a significant increase in nonelastic resistance of the lungs—the mean resistance was 37 cm. H_2O/sec. in controls and 157 cm.H_2O/sec. in exposed animals. The physiologic changes were virtually reversed when several survivors were given fresh air after 3 months of NO_2 exposure; however, the main residual abnormality was the nonelastic resistance.

Dogs

Anesthetized dogs exposed to 13 to 190 p.p.m. (25 to 358 mg./m.^{3}) NO_2 for 25 or 40 minutes or to 2 to 199 p.p.m. (4 to 374 mg./m.^{3}) for 20 minutes exhibited a significant increase in ventilatory work from the end of the exposure to 30 minutes thereafter (*27*).

Laboratory Animals

Several experiments were conducted with rats to determine the overall effects of NO_2 toxicity. Some of the references on rats will be reviewed briefly, because of the possible applicability to domestic animals.

Physiological changes

Exposure to NO_2 (up to 0.5 p.p.m. or an equivalent of 0.9 mg./m.^{3}) for 2 through 6 weeks resulted in increased blood catalase values of rats at the fifth week but lowered values at the sixth week and a significant increase in aspartic acid excretion (*20*).

Chronic exposure of rats to 0.84 and 5.7 mg./m.^{3} of NO_2 for 6 months elicited clear-cut changes in the conditional reflex activity, more so at the higher level. After 5 months of chronic exposure at the higher NO_2 concentration, rats began to lose fur over the spinal area (*26*).

Chemical changes

Exposure of rats to 1 p.p.m. (1.9 mg./m.^{3}) NO_2 for a single 4-hour period or for 4 hours daily in a 6-day period produced peroxidative changes of lipids in lungs by the 18th hour after exposure; the peak was reached between 24 and 48 hours after exposure (*25*). The changes were formations of a conjugated diene and of ketone or aldehydic dienes. The prooxidant effect of NO_2 in rat lungs could be partially prevented by prior treatment of rats with large doses of α-tocopherol at the rate of 10 mg./day/animal for 3 days (*21*). All cell types from rat and mouse lung tested in vitro showed a partial but reversible inhibition in oxidative activity during treatment with $NaNO_2$; cell structure changes were noted via the electron microscope.

Toxicity of various nitrogen oxides

Exposure of rats to vapors of NO_2, red fuming HNO_3, and white fuming HNO_3 from 2 minutes to 4 hours showed that the primary toxic constituent of the acids was NO_2; the LC_{50} was 138 and 67 p.p.m. (259 and 126 mg./m.^{3}) NO_2 for 30 and 240 minutes, respectively (*15*).

A direct relation between room temperature and the toxicity of NO_2 was demonstrated with rats (*15*). Similar results (*18*), with one exception, were observed with mice in which the survival time at 10°, 15°, 20°, 22°, 25°, 30°, and 35° C. was approximately 50, 60, 50, 46, 44, 25, and 20 minutes, respectively. The toxicity was greater below and above 15° because of increased methemoglobin formation and thermoregulatory disturbance below 15° and because of heat regulatory disturbance and reduced O_2 consumption above 15°. During exposure to the gas, the mice exhibited washing movements, closed eyelids, unsteady gait, skin cyanosis, mucous discharges from nose and mouth, convulsions, and many of the mice died.

NO_2 and HNO_3 vapor had a much lower lung-irritant action than N_2O_5 in inhalation studies with rats; the results suggested that N_2O_5 reacted directly with some constituent of pulmonary tissue rather than derived the toxicity from nitric acid (*12*).

Species Differences

Rats and dogs were exposed for single 5- to 60-minute periods to various concentrations of NO_2 (*4*). Lung to body weight ratios of rats correlated directly with the severity of NO_2 exposure; the kidney to body weight ratios of rats nor the hematocrit value and blood-platelet counts of dogs were of little or no value in evaluating the severity of NO_2 exposures; dogs showed only mild toxic signs at NO_2 concentrations that caused pulmonary edema in rats. Based on lung to body weight ratios of rats and the pathological changes found, the concentrations of NO_2 at which no effects were found were 104, 65, and 28 p.p.m. (196, 122, and 53 mg./m.^{3}) for 5, 15, and 60 minutes, respectively.

Studies with rats, guinea pigs, Swiss albino mice, inbred mice, hamsters, rabbits, dogs, and monkeys indicated that the effects of NO_2 exposure were restricted almost exclusively to the respiratory tract (*13*, *22*). With increasing dosage, the progressive effects of NO_2 were odor perception, nasal irritation, difficulty in breathing, acute respiratory irritation, edema, and death (*13*). Concentrations of 5 to 20 p.p.m. (9 to 38 mg./m.^{3}) NO_2 and 25 to 35 p.p.m. (47 to 65.8 mg./m.^{3}) produced pathological changes in the lungs of laboratory animals and of monkeys, respectively (*13*). Cumulative 30-, 60-, and 90-day mortality data indicated that the 30-day results do not necessarily anticipate the effects that might occur after 90 days (*22*).

NO_2 exposure for 2 hours reduced resistance to *Klebsiella pneumonia* infection; only 3.5 p.p.m. (6.6 mg./m.^{3}) were needed for mice to succumb to infection when exposed to *K. pneumonia*, as contrasted with 35 p.p.m. (65.8 mg./m.^{3}) for hamsters and monkeys (*13*).

EXPOSURE TO NITROGEN OXIDE INHALATION VIA TRACHEA IN THE LABORATORY

Several heifers were fitted with a tracheal cannula; daily doses varied from 2,500 to 6,000 ml. of NO_2, and the exposure time was 5 minutes. Death occurred between 11 and 25 days after initial exposure. Two other heifers were forced to inhale NO_2 (doses not measured)—one for one single exposure of 1 to 2 minutes and the other one for four exposures (1 to 2 minutes per exposure) in a 15-day period; death occurred on the third day and on the 15th day for the single-exposed and multiple-exposed heifer, respectively. During exposure, excitement and violent struggling were greater in heifers exposed to forced inhalation than via the trachea. The clinical signs were apnea, progressive dyspnea, lacrimation, excessive salivation, grunting, reduced feed and water consumption, emaciation, and dehydration. The hematological findings were an increase in lymphocytes and a decrease in neutrophils. The pathological results included methemoglobinemia, severe dyspnea, dark red kidneys, necrosis of skeletal muscles, and pulmonary lesions such as hyperemia, edema, hemorrhage, fibrin deposition, hyperplasia, bronchiolitis, infarcation, and emphysema. These findings suggested that NO_2 was not the cause of bovine pulmonary adenomatosis (*7*, *8*).

METHODS

KI-starch papers, available from chemical supply companies at a negligible cost per vial, may be used by farmers to detect the presence of NO_2 in silos. Moistened test paper placed a few doors high in the silo chute will turn deep bluish black within a few seconds if NO_2 is present (*11*).

SUMMARY

In the field, nitrogen oxide poisoning cases have been restricted to silos on farms where farmers, cattle, swine, poultry, and even flies died almost instantly when passing by the open silo chute door. The minimum lethal levels of silo-originated N oxides have not been established for domestic animals. Deaths among farm animals and farmers can be prevented largely by proper management practices both in the growing season of crops to be ensilaged and at the time of ensilage.

When first exposed to nitrogen oxide gases in the field as well as in the laboratory the animals begin to pant followed by excessive salivation, lacrimation, dyspnea, mucous discharge from nose and mouth, a loud grunt, reduced feed and water consumption, and death. The physiological, chemical, and pathological changes involved methemoglobinemia, pulmonary lesions, peroxidative changes of lipids in rat lungs, reduction in resistance to *K. pneumonia* infection in mice, increase in the nonelastic resistance

of lungs in rabbits, necrosis of striated muscle, and loss of fur over the spinal column of rats chronically exposed to NO_2 for 5 months.

Of all the nitrogen oxides tested in the laboratory, NO_2 was the primary toxic constituent of the acids. In most cases, the toxicity of NO_2 increased with a corresponding increase in the ambient temperature.

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Chapter 20.—Ozone

Ozone (O_3) is an oxidizing agent used in industry as a bleach for oils, waxes, ivory, flour, and starch, as a deodorizer in air purification processes, as a water sterilizer, and as a food preserver. However, O_3 has become a dominant constituent of photochemical smog as a result of the interaction of automobile exhaust, industrial smoke waste, and other organic substances in the presence of sunlight (*5*). The biological effects of O_3 on man and animals have been comprehensively reviewed (*3, 7, 8, 19, 21, 22, 23*). These reviews have indicated a paucity of information on domestic animals.

EXPOSURE TO O_3 INHALATION IN THE FIELD

Measurements of O_3 content in the air were made both inside and outside an animal barn in the evening when the stable chores were completed and in the morning before the chores began (*9*). The animals housed in the barn were six rams, three bulls, and two horses. The data revealed insignificant quantities of O_3 in the barn air, irrespective of the O_3 concentration in the outside air. Further studies (*9*) with two barns, one empty and the other occupied by animals, confirmed the results that disintegration of O_3 was quicker in the presence of animals.

EXPOSURE TO O_3 IN THE LABORATORY

Poultry

Hatching Leghorn eggs were exposed continuously to concentrations of 1 to 4 p.p.m. (2 to 7.9 mg./m.^{3}) of O_3 (*18*). The hatchability of these eggs was unaffected, probably because of the failure of O_3 to reach the embryo. However, the chicks hatched from the exposed eggs exhibited between 50 and 99 percent mortality after 5 days of continuous exposure. The concentration-time value for an LD_{50} exposure for chicks was 53.5 p.p.m.-hours in individual cages; no evidence of tolerance on re-exposure of chicks to O_3 could be demonstrated. However, in another study (*1*), ozonization in poultry incubators improved embryonic viability by 3 to 5 percent, and these treated incubators produced more vigorous chicks than untreated incubators.

Goats

Exposure of goats to 15 to 20 p.p.m. (29.4 to 39.3 mg./m.^{3}) O_3 for 2 hours produced death. Before death, the symptoms were coughing, headache (how was this determined?), and inflammation of the respiratory tract including edema (*6*). Goats exposed to 7 p.p.m. (13.7 mg./m.^{3}) O_3 for $3\frac{1}{2}$ hours or to $9\frac{1}{2}$ p.p.m. (18.6 mg./m.^{3}) O_3 for between 3 and $3\frac{1}{2}$ hours exhibited dyspnea with moist sounds and depression; all recovered when given fresh air (*19*). No evidence of O_3 was present in the expired air, a fact indicating that O_3 was absorbed by the wet mucous surface of the respiratory tract (*6, 19*).

Cats and Dogs

Death usually resulted from exposure for 2 hours to 15 to 20 p.p.m. (29.4 to 39.3 mg./m.^{3}) O_3 in cats and dogs. As little as 1 p.p.m. (2 mg./m.^{3}) O_3 was irritating to the respiratory tract (*6*).

Species Differences

The LD_{50} for a 3-hour exposure of O_3 was found to be 21, 21.8, 34.5, 36, and 51.7 p.p.m. (41, 43, 68, 71, and 102 mg./m.^{3}) for mice, rats, cats, rabbits, and guinea pigs, respectively (*16*). Edema occurred in lungs of rats exposed to 6 p.p.m. (12 mg./m.^{3}) for 18 hours; no damage was caused by 24-hour exposures to concentrations of less than 3 p.p.m. (6 mg./m.^{3}) O_3.

Mice, rats, hamsters, guinea pigs, and dogs were exposed to 0.5 to 2.34 p.p.m. (1 to 4.6 mg./m.^{3}) O_3 for 6 hours daily, 5 days per week for 433 days (*24*). This chronic exposure produced bronchitis and bronchiolitis (thickened terminal airways of lungs, narrowed air passages, fibrosis, emphysema) in all species except the dog. The only symptom observed in the dogs was mild irritation of the trachea and major bronchi.

EXPOSURE TO O_3 FROM UNFILTERED AND FILTERED URBAN ATMOSPHERES AND FROM A SYNTHETIC ATMOSPHERE

Three groups of mice were exposed to (a) the urban atmosphere with its daily variations in pollutant concentration (control), (b) the urban atmosphere in a filtered state, and (c) a synthetic pollutant atmosphere made up of a smog created by reaction of gasoline with O_3 (*11*). The results showed that the synthetic smog significantly reduced the ability of mice to conceive, decreased size of litters, and increased mortality to almost 100 percent in progeny before weaning. No differences were observed between the unfiltered and filtered urban atmospheres. The synthetic smog also significantly increased the incidence of pulmonary tumors (neoplasm) in inbred mice (*10*).

MISCELLANEOUS

A preponderance of the literature on the biological effects of O_3 referred to laboratory animals. A few of these references will be reviewed briefly, because of the possible applicability to domestic animals.

Resistance to Disease

Exposure of laboratory animals, challenged with streptococcus bacteria or *Klebsiella pneumoniae* bacteria, to various levels of O_3 caused a significant enhancement in mortality, as compared with disease-challenged animals not exposed to O_3 (*2, 7, 17*).

Tolerance to O_3 Toxicity

Development of tolerance to O_3 has been demonstrated by a number of investigators. The findings reported by these investigators have been summarized in general terms by another investigator (*19, 20, 22*) as follows: factors that increase the toxicity of O_3 are young age, higher temperature, increased exercise, increased dosage rates, poor health, continuous rather than intermittent exposure, and absence of reducing agents and drugs. Three long-term effects from chronic O_3 toxicity are chronic pulmonary effects, aging, and lung-tumor acceleration. Chronic bronchitis, bronchiolitis, and emphysema have occurred after 1 year in small laboratory animals exposed daily to around 1 p.p.m. (2 mg./m.^{3}) O_3; whereas, dogs showed none of the deep-lung changes (*22*).

Neonatal thymectomy of male white Swiss mice did not protect the mice preexposed to sublethal doses of O_3 from a subsequent lethal dose of O_3 (*4*). Hence, the thymus or some function dependent on the gland was necessary during maturation for the development of tolerance to O_3.

Alleviators

The alleviators that were protective against O_3 toxicity were ascorbic acid (*12, 15*), atropine sulfate and sodium thiosulfate (*15*), and serotonin (*13*); those that were ineffective were hydrocortisone (*12*), glutathione and p-aminopropiophenone (*15*), and oxygen, oxygen–helium gas mixtures, silicone aerosols, and various antifoams (*14*).

SUMMARY

No information was available on the biological effects of O_3 on farm animals in the field other than the disintegration of O_3 in the stable air only in the presence of animals. In the laboratory O_3 toxicity had been demonstrated with goats, dogs, cats, and newly hatched chicks; however, ozonization reduced the mortality of swine, improved the hatchability of chicken eggs, and increased the vitality of young chicks.

A comparison of O_3 in the unfiltered and filtered urban atmospheres and in a synthetic atmosphere revealed that the synthetic atmosphere significantly affected the reproductive efficiency and subsequent progeny performance in mice. Animals already challenged with pathogenic bacteria exhibited a higher mortality in the presence than in the absence of O_3 exposure.

Factors that increase O_3 toxicity are young age,

higher temperature, increased exercise, increased dosage rates, poor health, continuous rather than intermittent exposure, and absence of reducing agents and drugs. Three long-term effects from chronic O_3 toxicity are chronic pulmonary effects, aging, and lung-tumor acceleration. Dogs appeared to be more resistant than small laboratory animals. Some of the effective alleviators in protection of animals against O_3 toxicity are ascorbic acid, atropine, and sodium thiosulfate. The thymus gland or some function dependent on the gland is apparently necessary for the protection of mice pre-exposed to sublethal doses of O_3 from a subsequent lethal dose.

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Chapter 21.—Sulfur Oxides

Sulfur dioxide (SO_2) and sulfur trioxide (SO_3) are the two sulfur oxides (SO_x) of greatest concern in air pollution. The combustion of coal, oil, and gas in industry, vehicles, and residences is the chief source of SO_x being emitted into the atmosphere; another source is volcanic gases. In Hawaii damage due to sulfur gases from volcanic eruption was evident in fields of sugarcane 20 and 30 miles away from the eruption, but not between these two areas; no mention was made regarding the effects on animal life in these areas (*10*). A preponderance of literature dealt with SO_x damage on crops. Very little information was available on the biological effects of SO_x on domestic animals, other than during the major air pollution episodes. Results obtained with SO_2 on laboratory and domestic animals have been briefly reviewed (*2*, *3*, *13*, *23*, *24*).

EXPOSURE TO SO_X INHALATION IN THE FIELD

The cause of the symptoms found in the Meuse Valley in 1930 and in the London fog of 1952–53 was believed to be SO_2 (*1*, *16*, *17*). The symptoms were severe respiratory distress culminating in pneumonia, bronchitis, or influenza among humans, mostly under 1 year and over 45 years of age. Deaths were high among cattle; many had to be slaughtered. In one case, farmers led the cattle from the Meuse Valley to bordering hills above the dense fog, after which the respiratory symptoms ceased. Later investigation convinced several researchers that deaths in humans and cattle in the London fog of 1952 was attributed to a combination of SO_2 and H_2SO_4 mist as well as other toxic agents (*11*, *14*). Another investigator (*22*) believed that fluorine (F) rather than SO_2 was the culprit for the disaster in the Meuse Valley, because 15 out of 27 factories in the valley used raw products containing F, hence F emissions.

EXPOSURE TO SO_X INGESTION IN THE FIELD

Cattle

In a 90-day double reversal feeding trial (*15*), 10 cows were fed a ration of mixed grain, corn silage, and either uncontaminated or contaminated alfalfa hay (the contamination resulted from SO_2 emissions into the atmosphere from an industrial plant). Results obtained with milk production, body-weight changes, apparent digestibility of the rations, palatability, and pH of urine indicated no significant change in cows fed alfalfa hay with more than 25 percent of the leaflets damaged by SO_2.

Other Farm Animals

H_2SO_4 fumes formed from the SO_2 emissions of a factory contained 1 to 4.5 percent (10,000 to 45,000 p.p.m.) SO_2 that was deposited on vegetation; this contaminated vegetation that contained 1,760 to 2,470 p.p.m. of H_2SO_4 poisoned livestock grazing in the area (*4*).

EXPOSURE TO SO_X INHALATION IN THE LABORATORY

Swine

Young swine under 7 days of age were exposed via nose to SO_2 concentrations of 5, 10, 20, and 40 p.p.m. (13, 26, 38, and 105 mg./m.^{3}) for a single 8-hour period (*21*). Slight eye irritation and salivation occurred on the 5 p.p.m. level; eye irritation, nasal secretion, salivation, and altered respirations on the higher levels; and hemorrhage and emphysema within 24 hours at the 40 p.p.m. level. At 158 days postexposure, two out of two swine exposed to 40 p.p.m. and one out of two to 20 p.p.m. showed a pulmonary fibrosis attributable to SO_2. The potential hazardous effects of SO_2 could be influenced by temperature, relative humidity, and ventilation rate; farmers believed that greatest damages occurred in cold weather.

Rabbits

Exposure of rabbits via nose to 0.4 mg./l. (400 mg./m.^{3}) of SO_2 for 6 hours daily for 4 successive days resulted in a sharp drop in blood vitamin C levels by 50 percent in most cases (*7*). However, prolonged exposure (9 successive days) produced a preliminary rise in the blood ascorbic acid ($2\frac{1}{2}$ to 3 times as much), followed by a sharp fall by the fifth day after exposure.

Dogs

Dogs were prepared so that an isolated segment of the trachea could be perfused with radioactive $^{35}SO_2$ gas–air mixture without the gas entering the main stem bronchi or lungs (*9*). When inhaled through the nose and mouth in concentrations as low as 1 p.p.m. (2.6 mg./m.^{3}), at least 90 percent SO_2 was removed from the gas–air mixture and became localized mainly in the pharynx, trachea, lungs, and hilar lymph nodes. The SO_2 conversion products containing S were taken up from these sites of deposit and distributed to all tissues, including brain; a significant amount was found in the liver, spleen, and kidneys. The SO_2 found in the trachea and lungs was slowly removed and could be detected in these sites 1 week after exposure.

Laboratory Animals

Exposure to SO_2

Resistance to disease.—The depressing effect of SO_2 on immunobiological activity was reported with rabbits exposed to SO_2 inhalation before or after vaccination. The concentrations of SO_2 used were 0.018 to 0.022 mg./l. (18 to 22 mg./m.^{3}) (*20*) and 20 mg./m.^{3} (*8*).

Physiological changes.—Exposures of white rats to SO_2 concentrations of 0.1, 0.5, or 20 mg./m.^{3} for approximately 4 hours per day for 1, 114, 144, or 165 days resulted in a decrease in the activity of certain enzymes such as cholinesterase, spleen dehydrase, and carbohydrase and in the vitamin C content of several organs (*18, 19*). When rats were repeatedly exposed to radioactive SO_2 inhalation, the data (*12*) suggested that the SO_2 conversion products containing S tended to accumulate in the body organs, more so in the lungs than in other organs; this accumulation could develop pathological processes in the organism.

Exposure to H_2SO_4 (SO_3)

Lethal and pathological effects.—Concentrations of 22.1, 140, 178, and 296 p.p.m. (89, 561, 714, 1,186 mg./m.^{3}) were required to kill guinea pigs, mice, rats, and rabbits, respectively; the length of time required to produce death at these concentrations was 2.75, 3.5, 7, and 103 hours, respectively. The pathological effects of H_2SO_4 mist inhalation were degenerative changes of epithelium of the respiratory tract, pulmonary hyperemia, edema, emphysema, atelectosis, and sometimes focal pulmonary hemorrhages (*26*).

Effect of particle size.—When the H_2SO_4 mist was supplied in three particle sizes (coarse, medium, fine), the fine particle H_2SO_4 aerosol (0.8 μ) was most effective of the particle sizes in producing respiratory distress in guinea pigs at small concentrations (2 mg./m.^{3}), the medium particle size (2.5 μ) was more effective than the fine particle size only at high concentrations (40 mg./m.^{3}), and the coarse particle size (7 μ) produced only a slight response even at high concentrations because this size did not penetrate beyond the upper respiratory tract (*5*). Conversely, medium-sized aerosols (0.9 μ) were more active than either the fine (0.6 μ) or coarse (4 μ) aerosols in producing histological alterations in guinea pigs exposed to H_2SO_4 mist concentrations from 0.20 to 12.7 mg./m.^{3} (*25*).

Comparison between SO_2 and H_2SO_4

H_2SO_4 mist is more toxic than SO_2(*14*) and has two distinct toxic actions; namely, laryngeal spasm and deep-lung damage (*6*). The laryngeal spasm is the cause of high mortality. The severity of lung damage is dependent on total dosage rather than concentration alone.

SUMMARY

This survey indicated a paucity of literature on SO_2 with domestic animals. One feeding trial indicated that feeding of alfalfa hay with more than 25 percent of the leaflets damaged by SO_2 had no effect on the overall performance of cows. Swine exposed to several concentrations of SO_2 exhibited eye irritation, salivation, nasal secretion, altered respiration, hemorrhage, emphysema, and pulmonary fibrosis.

The physiological and pathological observations in laboratory animals exposed to SO_2 included decreased activity of certain enzymes, a drop in the vitamin C content of blood and other organs, and depressed immunobiological activity. H_2SO_4 (SO_3) appeared more toxic than SO_2, and the toxicity was influenced by the particle size of the aerosol. The toxic effects of H_2SO_4 were two distinct types: laryngeal spasm and deep-lung damage.

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Chapter 22.—Vanadium

Vanadium (V) has been used as a catalyst in the production of sulfuric acid. The literature survey revealed a paucity of data on V toxicosis in the field. Several references on research conducted in the laboratory will be discussed herein to provide a general background of V toxicity that might possibly apply to domestic animals in the field.

EXPOSURE TO V INGESTION IN THE FIELD

Several cows exposed to soot dispersed over the grazing area began to exhibit weakness and ataxia (*4*). Hematological findings revealed V toxicity; the V content of soot, liver, and kidney was 1, 1.5 to 2.4, and 3 to 4.7 p.p.m., respectively; that of urine was 2.85 p.p.m. These data emphasize the importance of proper handling of fuel oil soot.

EXPOSURE TO V INGESTION IN THE LABORATORY

Cattle

Ten bull calves 6 months old were given daily for 1 month or until death 1, 3, 5, 7.5, 10, 15, or 20 mg. V/kg. body weight as ammonium metavanadate in gelatin capsules (*7*). The first four concentrations produced no clinical symptoms; the next three higher levels began to produce symptoms 14, 6, and 3 days after initiation, respectively. The clinical symptoms before death included weakness, diarrhea, gradual loss of appetite, emaciation, lethargy, drier hair, and prostration. The main gross pathological changes were: liver and lung congestion, diffuse petechia covering the kidney and heart muscle, mycotic lesions in rumen, hemorrhage of intestine, and granulation tissue in testicles. No changes were observed in the hemotological value or in the central nervous system. Tissue analysis showed greatest concentration of V in kidney, followed by liver and spleen and none in blood, lungs, skeletal muscle, or testicles.

Chickens

Young chickens

When V was fed at various levels in practical and purified diets, the levels required to depress growth of chickens were 13, 25, 30, and more than 35 p.p.m. (*1, 3, 6, 8*). In mortality studies, 25 p.p.m. in a purified diet and 200 p.p.m. in a practical diet produced high mortality (*3, 8*).

Both ammonium metavanadate and vanadyl sulfate were equally toxic (*3*). The addition of essential trace minerals (Fe, Cu, Mo, Co, Zn, Mn) did not affect the toxicity of V in rations. Scandium, titanium, and niobium, all of which resemble V in many chemical and physical parameters, were not toxic when fed at 200 p.p.m., nor did they influence the toxicity of V.

Laying hens

When (*2*) layers were fed V as ammonium vanadate in concentrations from 0 to 100 p.p.m. in an 8-week period, 15 to 20 p.p.m. depressed albumen quality; 30 p.p.m. depressed egg production; and 50 p.p.m. depressed hatchability. Body weight tended to be depressed in a linear nature as the level of V in the diet increased.

Rabbits

The addition of V as V_2O_5 at the rate of 50 or 100 p.p.m. in the diet of rabbits up to 150 days, either with or without 1 percent dietary cholesterol indicated (*5*) the following results: (a) 100 p.p.m. V without dietary cholesterol lowered free cholesterol and phospholipid content of rabbit livers but plasma cholesterol showed no significant changes, (b) 50 p.p.m. V plus 1 percent cholesterol restricted the elevation of free and total cholesterol levels of plasma. The data suggested that inhibition of cholesterol synthesis and accelerated catabolism of cholesterol were involved in the mechanism by which V restricts elevation of plasma cholesterol.

EXPOSURE TO V INHALATION IN THE LABORATORY

Exposure of rats to chronic inhalation of 0.003 to 0.005 mg./l. (3 to 5 mg./m.^{3}) of V_2O_5 2 hours every other day for 3 months or 0.01 to 0.03 mg./l. (10 to 30 mg./m^3) 1 hour daily for 4 months resulted (*9*) in hyperemia of lungs, passive behavior, loss of weight, disturbance of circulatory system, vasodilation, and blood stasis in vessels of internal organs; no differences were observed in the general health of treated and control animals. Acute V toxicity that proved lethal was 0.07 mg./l. (70 mg./m.^{3}) V_2O_5. Aerosol inhalation was much more toxic than dust inhalation.

SUMMARY

A minimum of 7.5 mg. V/kg. body weight administered daily in gelatin capsules produced adverse effects in bull calves 14 days after initiation. The effects were weakness, diarrhea, emaciation, lethargy, drier hair, death; liver and lung congestion, lesions, and hemorrhage were some of the pathological changes. Vanadium was found in greatest concentration in kidney, followed by liver and spleen; none was found in blood, lungs, skeletal muscle, or testicles.

With growing chickens, the toxic levels for growth and mortality varied from 13 to 35 p.p.m. and 25 to 200 p.p.m., respectively. For layers, 15 to 20 p.p.m. affected albumen quality, 30 p.p.m. depressed egg production, and 50 p.p.m. lowered hatchability. No clinical and pathological observations were made on the tissues of chickens.

A relation between dietary V and dietary cholesterol was demonstrated in rabbits. Exposure of rats to chronic V inhalation produced hyperemia of lungs, passive behavior, and disturbance of the circulatory system; however, no differences were observed in the general health of treated and untreated rats.

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Chapter 23.—Zinc

Zinc (Zn) is a volatile metal used in galvanizing iron plumbing fixtures, iron fence netting, roofing materials, and other iron products to prevent rust corrosion. This metal is one of the several metals being emitted into the atmosphere by copper smelters as well as other smelters (*2*). Effects of Zn and other metals from industrial emissions on animals were very briefly discussed (*1*, *4*). One case (*3*) of Zn poisoning occurred on a Swedish farm, in which the welding of galvanized iron piping produced a white smoke that spread throughout the barn containing 60 cattle. On the second welding day, a cow in advanced pregnancy became ill and died 12 hours later of dyspnea. Autopsy revealed pulmonary emphysema. On the same day, seven other cows in advanced pregnancy sickened with the following symptoms: increased body temperature (104° F), increased pulse (100), and increased respiration (90 per minute). The welding was stopped, and the barn completely aired out, after which the sickened cows rapidly recovered. The investigator claimed that the white smoke contained Zn fumes that caused the poisoning of cattle. A value of 15 mg./m.^{3} of ZnO was recommended as the maximum permissible concentration for cattle grazing in the vicinity of large industrial plants (*5*).

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Chapter 24.—Combination of Air Pollution Mixtures

A combination of two or more air pollutants could produce an antagonistic, a synergistic, or a neutral effect on animals (*34*, *39*). Specific examples of the biological effects on mostly laboratory animals exposed to a combination of certain air pollutants not discussed in previous chapters will be described herein.

AEROSOLS

Effect of Particle Size

The smaller the particles of an aerosol, the greater was the potentiating effect on the response to certain air pollutants (*3*, *4*, *5*, *7*). With NaCl aerosols, the potentiating effect was positive with SO_2 (*3*, *4*) and with formaldehyde (*4*, *5*), and negative with acetic acid (*4*) and with formic acid (*4*, *5*).

The bacteriological irritation analogue test was used as an indicator for the degree of association of the irritant gas with airborne particulate matter by comparative tests before and after passage through the aerosol spectrometer (*25*). The findings revealed a harmful synergistic effect between the irritant gas and particle surfaces; this synergistic effect paralleled the pattern of tests with laboratory animals by other investigators. Hence, bacteria could be used instead of animals or man for such studies.

Soluble Versus Insoluble Aerosols

Soluble aerosols (Mn, Fe, V) potentiated the response to SO_2 much more rapidly and at much lower concentrations of aerosol than with NaCl; the insoluble aerosols (fly ash, activated carbon (C), spectrographic C, triphenyl phosphate) were completely ineffective (*6*).

Comparison of Several Aerosols

NaCl, KCl, and NH_3 thiocyanate ranked in that order of potentiating the response to SO_2 (*6*).

Pathogenic-Containing Aerosols

An unfavorable synergistic effect occurred when mice exposed to O_3 or NO_2 were challenged with a *Klebsiella pneumoniae* bacterial aerosol (*21*). Conversely, a challenge with a Newcastle disease viral aerosol had no potentiating effect on chickens exposed to a combination of dust and NH_3 (*8*).

Physical Effects of Aerosols

The addition of aerosols to atmospheres containing formaldehyde vapors, nitric acid fumes, or acrolein vapors increased, decreased, and neither increased nor decreased the toxicity in mice, respectively (*28*). When the aerosol penetration exceeded vapor penetration, toxicity was increased; when vapor penetration exceeded particle penetration, toxicity was decreased. Hence, a physical combination between vapor and aerosol must be present or no change would occur.

NH_3 WITH OTHER IRRITANTS

NH_3 and H_2SO_4

The presence of NH_3 from droppings reduced the toxicity of H_2SO_4 mist (*14*). This factor might explain why sheep and swine did not die in the Smithfield London Show, but cattle died—simply because the cattle were kept very clean at all times, hence no NH_3.

NH_3 and C

A combination of 119 p.p.m. (82.7 mg./m.^{3}) NH_3 and pulverized C particles (3.5 mg./m.^{3}) produced a harmful synergistic effect on the ciliary activity and on the trachea of rats (*17*).

NH_3 and Dust

When turkeys were exposed to NH_3 in the presence of dust, no synergistic effects were observed on feed conversion, mortality, and air-sac lesions; however, synergism caused a loss of ciliary activity, an increase in mucus-secreting goblet cells, and in most cases consolidation and inflammation of lungs (*9*).

Be WITH OTHER IRRITANTS

A combination of $BeSO_4$ and HF enhanced the toxicity of Be and increased F deposition in teeth and bone of rats (*40*).

C WITH OTHER IRRITANTS

Inhalation of C (18,000 to 21,000 particles/m.^{3}) 4 hours/day three times a week produced a macrophage response in alveolar spaces of lungs in guinea pigs; inhalation of NO_2 (25 p.p.m. (47 mg./m.^{3}) for 2 hours/day or 75 p.p.m. (141 mg./m.^{3}) for a 2-hour exposure/week) caused pulmonary edema in acute cases and minimal lung destruction in long-term studies (2 years) (*10*). However, C inhalation followed by NO_2 inhalation produced lung destruction, whereas the reverse combination did not; hence, C inhalation is believed to prime the lungs for subsequent damage when exposed to other air pollutants.

CO WITH OTHER IRRITANTS

CO and SO_2

A combination of CO and SO_2 in equal parts depressed considerably the activity of succinic dehydrogenase in the parenchymal organs of rabbits, more than CO alone (*35*).

CO and NO, NO_2, or O_3

The carboxyhemoglobin values of rats and mice are primarily dependent upon the atmospheric CO concentration and not significantly affected by the simultaneous atmospheric presence of NO, NO_2, or O_3 (*29*).

HC WITH OTHER IRRITANTS

HC and Nitrogen Oxides

A combination of HC and nitrogen oxides appeared to be more irritating than either one alone, especially at low concentrations (*27*).

HC and Ultraviolet Light

Treatment of living, human conjunctival cells in vitro with a combination of a chloroform extract of auto exhaust and a 5-minute exposure to ultraviolet light induced cytolosis within 2 hours, but cytolosis was not induced with either one alone (*37*).

HC and O_3

Preexposure to ketene protected mice against lethal O_3 doses and vice versa (*30*).

HC Antagonists

Injection of a vitamin mixture (ascorbic acid, sodium nicotinate, riboflavin) largely, if not completely, protected cats and rats from orthonitrochlorobenzene poisoning (*26*).

H_2S WITH OTHER IRRITANTS

Exposure of rabbits to a mixture of H_2S and CS_2 (carbon disulfide) produced a decrease in albumin and albumin-globulin ratio and an increase in globulin. Restoration to normal after gas inhalation withdrawal was slow and not complete (*45*).

O_3 OR NITROGEN OXIDES, OR BOTH, WITH OTHER IRRITANTS

The tolerance mechanisms of O_3 with other irritants were reviewed in general (*22*). The toxicity of O_3 was increased by nitrogen oxides with rats and mice (*19*) and by high concentrations of H_2O_2 with mice and rats (*43*). No additive effects were observed with O_3 and nitrogen oxide mixtures (*38*) or with O_3 and HC combinations (*16*). Preexposure to O_3 protected the mice from lethal effects of challenging air pollutants such as ketene, NO_2, or a mixture of O_3 and H_2O_2; preexposure to ketene, NO_2, or O_3-H_2O_2 mixture protected the mice from lethal doses of O_3 or NO_2; hence, a cross-tolerance (*41*).

The degree of antagonism produced by oil mists against O_3 or NO_2, or both, depended on five factors: time of treatment, duration of treatment, sequence of oil and oxidant, type of oil, and type of oxidant (*44*). Two distinct but related pathways of protection against the lethal effects of O_3 and NO_2 in mice were shown by (a) simultaneous inhalation of compounds that contain one or both of the sulfur groups (—SH or —SS—) and (b) by injection of thiourea derivatives several days before exposure to the oxidants (*24*).

SULFUR COMPOUNDS WITH OTHER IRRITANTS

SO_2 and As_2O_3

Feed grown near foundries in Germany showed a high SO_2 and As content; cattle in these contaminated areas became stunted and sterile and exhibited osteomalacia or osteoporosis as a result of Ca deficiency (*31*).

SO_2 and H_2SO_4

A combination of SO_2 and H_2SO_4 produced a growth depression, a very marked respiratory response, and severe lung pathology in guinea pigs; these symptoms were not observed with either irritant alone (*2*).

SO_2 and Smoke

Smoke enhanced the toxic effects of SO_2 within the respiratory tract of guinea pigs and mice (*32*).

SO_2 and $ZnNH_3SO_4$

The irritant potency was more than additive in a mixture of SO_2 and $ZnNH_3SO_4$ than either one alone (*7*).

TRACE ELEMENTS WITH OTHER IRRITANTS

As and Pb

The combined effects of As and Pb poisoning in colts near a metal-working plant in Germany produced a strange illness with loosening of the cartilage and connective tissues of the spine (*42*).

Cu, Mn, and Pb

A combination of Cu, Mn, and Pb trace elements was the cause of poisoning and subsequent illness of sheep and cattle grazing near coke-oven factories (*20*).

INTERRELATIONS BETWEEN SEVERAL AIR POLLUTANTS

Cd and Zn

Both Cd and Zn are air pollutants that demonstrated a significant correlation with heart disease in humans. Although Cd and Zn are closely related elements, no information was available about the interrelations between the two elements (*11*).

H_2S, NH_3, CO_2 (Carbon Dioxide), and Methane

The fermentation process by which dung and urine form a liquid manure in animal enclosures increases the concentration of several gaseous compounds, principally H_2S, NH_3, CO_2, and methane

(*1, 12, 13, 15, 18*). The maximal values permissible according to DIN 18910 standards for barn air were 0.35, 0.01, and 0.002 vol. percent (6,299, 70, and 28 mg./m.^{3}) for CO_2, NH_3, and H_2S, respectively (*12, 13*). Agitation of the liquid manure, especially in pits, resulted in a sharp rise of H_2S and CO_2 gases above their DIN 18910 levels which became injurious to swine; after agitation, the H_2S levels declined more slowly than CO_2 to the acceptable levels (*13*).

The clinical symptoms of H_2S, NH_3, CO_2, and methane gases in swine are as follows (*15*): (a) methane becomes explosive in concentrations of 5 to 6 percent; (b) CO_2 produces palpitation at the 10-percent level and a narcotic action that often results in death at the 25-percent level; (c) NH_3 causes irritation of eyes and respiratory mucous membranes at the 0.01-percent level (70 mg./m.^{3}) and an 0.05-percent (348 mg./m.^{3}) level becomes a real health hazard; and (d) concentrations of 0.002 to 0.015 percent (28 to 209 mg./m.^{3}) H_2S irritate the eyes and produce dizziness within 30 minutes, a 0.05-percent (695 mg./m.^{3}) level affects the nervous system, and death occurs after 30 minutes of inhaling 0.09 to 0.1 percent (1,252 to 1,391 mg./m.^{3}) H_2S and instantly at higher levels.

H_2SO_4, N_2O_4, and Cl

Prolonged inhalation by dogs, guinea pigs, and pigeons of H_2SO_4, N_2O_4, and Cl in amounts exceeding 0.05, 0.05, and 0.002 percent (2,004, 1,881, 29 mg./m.^{3}), respectively, led to general nutritional deficiency coupled with a change in the main blood constituents, a decreased production of specific antibodies, a decreased production in the bacterial capacity of the lungs, and a decrease in disease resistance (*36*).

H_2S, SO_2, and NH_3

The order of decreasing toxicity of the gases to rats and mice was H_2S, SO_2, and NH_3 (*46*). The time, in minutes, at the 1,000 p.p.m. concentration (mg./m.^{3}: 1,391 H_2S, 2,618 SO_2, 696 NH_3), required to produce 50 percent mortality was 14 to 18 for rats and mice exposed to H_2S, 132 for mice and 910 for rats exposed to SO_2, and more than 960 for both species exposed to NH_3. The clinical symptoms varied somewhat for the three gases: H_2S produced violent activity and loss of muscular coordination at higher concentrations and less activity with irritation of eyes and nose and onset of pulmonary edema at lower concentrations; SO_2 caused little activity except for terminal convulsions, early signs of irritation of eyes and nose, and increasing signs of pulmonary edema; NH_3 resulted in very slight irritation of eyes and nose.

HORMONAL EFFECTS ON AIR POLLUTANTS

The feeding of 0.05 to 0.2 percent (500 to 2,000 p.p.m.) desiccated thyroid augmented the toxicity of fluorosis in the growing chick (*33*). Increased thyroid activity rendered mice highly susceptible to the action of O_3 and NO_2; whereas, chemical or surgical thyroidectomy significantly enhanced the survival of mice exposed to the lethal actions of both gases. Thyroid-blocking agents given simultaneously with thyroid hormone counterbalanced protective action of the former and augmented toxic action of the latter (*23*).

SUMMARY

The presence of several irritants in a given atmosphere usually produces a synergistic effect rather than an antagonistic or neutral effect. The degree of synergism or antagonism depends on several factors: size of particulates in the air, solubility of the compound, time and duration of treatment, sequence and type of irritant(s) or nonirritant(s), or both. Of the gases generated from liquid manure, H_2S and CO_2 are evidently more lethal than SO_2 and NH_3, especially with swine. The toxicity of certain air irritants can be enhanced by increased thyroid activity.

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Chapter 25.—Unclassified Air Pollutants

POLLENS

Normally a person breathes from 12,000 to 15,000 quarts of air per day; therefore, the importance of keeping the pollen count to a minimum cannot be overemphasized. The dispersion of ragweed pollen depends on the velocity of wind; at low velocities, the wind deposited 2,000 grains of ragweed pollen 20 feet from the plant, compared with 40 grains at 160 feet (*3*).

Although not thoroughly searched, no information could be found on the effect of pollens on domestic animals. However, the writer has seen dogs and cats sneeze many times.

AVIAN FECAL MATTER

Pigeons comprise the largest sized and most numerous avian infestations indigenous to metropolitan areas and represent the major source of avian fecal matter. Since uric acid represents approximately 80 percent of the avian fecal matter, particulate matter in the atmosphere was found to contain from 0.03 to 0.14 percent (300 to 1,400 p.p.m.) uric acid (*1, 2*). This concentration may seem rather insignificant; however, since the average daily air intake of man is 12,000 to 15,000 quarts, approximately 3 mcg. uric acid are inspired daily along with pathogenic germs transmitted to man by the pigeon—hence, a public health hazard.

AIRCRAFT POLLUTANTS

Diborane (B_2H_6) is now utilized in aircrafts and rockets as a high-energy fuel. As the concentration of B_2H_6 increased from 50 to 600 p.p.m. (35 to 417 mg./m.^{3}), the mean survival time for exposed hamsters decreased from 497 to 33 minutes (*4*). Higher levels elicited no further reduction in the mean exposure times for death. The pathological symptoms were confined to the lung areas—bright-red-colored lungs, capillary dilation, vascular congestion, edema, emphysema, and degeneration of mucosal cells. Some damage was apparent in kidneys only at the higher levels from 500 to 1,000 p.p.m. (348 to 695 mg./m.^{3}). (Note: It would be interesting to observe what effects the rocket gases would have on the performance of domestic animals grazing near rocket areas.)

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Chapter 26.—Summary and Conclusions

Of the air pollutants reviewed in this handbook, none have received more attention than fluorides, arsenic, and lead. The symptomology, tolerance limits, and alleviators have been well-defined for cattle and sheep afflicted with fluorosis, a disease that is worldwide. Arsenic was much more of a health hazard during the first 40 years of the 20th century than since then. Atmospheric lead, as differentiated from lead in pesticides and in materials such as paints and storage batteries, is recognized as a potential hazard. This is illustrated by the high lead content of vegetation and soils along heavily travelled roads. Nevertheless, no information could be found on the effect of high lead concentration on farm animals grazing along highways.

Other air pollutants commonly associated with domestic animals are: ammonia with poultry and swine; carbon monoxide with all domestic animals; dusts with poultry and rabbits; hydrogen sulfide with swine and poultry; sulfur dioxide with cattle, sheep, and swine; and nitrogen oxides with all animals. Little or no information was found on automobile exhausts, smoke, beryllium, cadmium, hydrocarbons, manganese, mercury, molybdenum, ozone, vanadium, and zinc affecting domestic animals in this country.

One striking observation in the literature search was effects of inhalation versus ingestion among grazing domestic animals exposed to atmospheric pollution. A preponderance of reports indicated that the ingestion of atmospheric-contaminated vegetation was the primary source of poisoning. However, reports suggested that inhalation of lead or uranium dust was more dangerous than ingestion of the same pollutants. Practically no information could be found to determine the degree of toxicity resulting from the inhalation of a pollutant and from the ingestion of vegetation contaminated by the same pollutant in the same animal at the same time.

The rank of decreasing susceptibility among domestic animals was demonstrated for cattle, sheep, horses, swine, rabbits, and poultry exposed to fluorosis, but the rank was not clearly demonstrated for domestic animals exposed to other air pollutants. No information was available on the susceptibility of dogs, cats, and honey bees in relation to other domestic animals exposed to fluorides. The literature search suggested that honey bees, although not directly compared, were more susceptible than ruminants to fluoride or arsenic. In several instances, where domestic animals were poisoned, humans were also affected.

The tolerance limits have not been established for domestic animals exposed to air pollutants except for fluoride with cattle, swine, and poultry and ammonia and carbon monoxide with poultry. Limited experimental studies with small numbers of farm animals exposed to one or more of the air pollutants showed in some cases deviation from the normal expectancy in the quantity or quality, or both, of eggs, milk, meat, and wool produced. The experimental studies also revealed discrepancies in the symptomology observed in the field. Many of these discrepancies are unavoidable because of the environmental differences in the composition of air contaminants during and after emission and in the meteorological conditions and also because of the presence or absence of interactions of many factors necessary to produce critical physiopathological situations. Other discrepancies are not unavoidable because in many cases the observations were made on only one or two animals in the field. Such data are not considered reliable or representative of the symptomology of a large population of afflicted domestic animals.

The health hazards associated with the polluted atmosphere have resulted in air pollution legislation in at least 30 States. Although this legislation is primarily intended for human beings, these controls should benefit the domestic animal. Despite industrial cooperation, emission of toxic air pollutants will continue to flow, although in lesser quantities, into the atmosphere. Consequently, proper animal husbandry practices and alleviators should be used to minimize the damages associated with chronic toxicosis of an air pollutant.

The question has come up about the percentage of domestic animals affected by air pollutants from an economic standpoint in the United States. The literature survey has indicated several major localized areas where a majority of complaints were received: the Montana-Washington-Utah area, the Tennessee area, and the Florida area. In these areas the trend of air pollution toxicity was not uniform because of the variables in meteorology and in industrial activity. Paradoxically, no major complaints regarding the health of domestic animals have been documented in the Los Angeles, the Chicago-Gary, and the New York-New Jersey boundary line areas where motorized traffic and industrial activity are very heavy. Inquiries from several agricultural statistical offices have shed no light on the statistical aspect of damage inflicted by air pollution on general domestic animal husbandry on a nationwide basis.

Hence, air pollution does not appear to constitute a major potential health hazard to domestic animals. However, the cadmium content of milk samples from 61 cities scattered throughout the United States revealed in some cases levels higher than the safe limit of 0.01 p.p.m. in drinking water for man. The source of Cd found in the milk samples was not specified, and no documentation of Cd poisoning in cattle was available before, during, or after the milk-sampling periods. This finding, coupled with evidence of higher concentrations of air toxicants in edible tissues of poisoned than of nonpoisoned farm animals, indicates the importance of establishing safe limits of toxic air contaminants found in the atmosphere, milk, eggs, meat, wool, honey, fruit, and vegetables for human beings and feedstuffs for farm animals.

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